**Applicant: Ranbaxy Pharmaceuticals (Pty) Ltd**
**Product Name:BOTIGEN 3,5**
**Dosage form: Powder for solution for injection**
**Strength: 3,5 mg Bortezomib ( as a mannitol boronic ester) per 10 mL vial**

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**Patient Information Leaflet**

**SCHEDULING STATUS: S4**

**BOTIGEN 3,5 (Powder for solution for injection)**

**Bortezomib** 3,5 mg (as a mannitol boronic ester) /vial

Contains sugar (mannitol 35 mg per vial)

**Read all of this leaflet carefully before you are given BOTIGEN 3,5:**

- Keep this leaflet. You may need to read it again.
- If you have any further questions, please ask your doctor, pharmacist, nurse or other healthcare provider.
- BOTIGEN 3,5 has been prescribed for you personally and you should not share your medicine with other people. It may harm them, even if their symptoms are the same as yours.

**What is in this leaflet**

1. What BOTIGEN 3,5 is and what it is used for

2. What you need to know before you are given BOTIGEN 3,5

3. How BOTIGEN 3,5 is given

4. Possible side effects

5. How to store BOTIGEN 3,5

6. Contents of the pack and other information

**1. What BOTIGEN 3,5 is and what it is used for**

BOTIGEN 3,5 contains bortezomib as the active ingredient and

belongs to a group of medicines called cytostatic medicines. These

are used to kill cancer cells.

BOTIGEN 3,5 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 and are unsuitable for high-dose chemotherapy with blood stem cell transplantation
- Alone or together with the medicines pegylated liposomal doxorubicin or dexamethasone, for patients whose disease is worsening (progressive) after receiving at least one prior treatment and for whom blood stem cell transplantation was not successful or is unsuitable.
- In combination with the medicines dexamethasone or dexamethasone together with thalidomide, for patients whose disease has not been previously treated and before receiving high-dose chemotherapy with blood stem cell transplantation (induction treatment).

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.
- In combination with the medicines rituximab, cyclophosphamide, doxorubicin and prednisone, for patients whose disease has not been previously treated and for whom blood stem cell transplantation is unsuitable.

**2. What you need to know before you are given BOTIGEN 3,5**

**You should not be administered BOTIGEN 3,5:**

- If you are hypersensitive (allergic) to bortezomib or any of the other ingredients of BOTIGEN 3,5.
- If you are hypersensitive (allergic) to mannitol or boron.
- If you have certain severe lung or heart problems

**Warning and Precautions**

**Tell your doctor or healthcare provider before being given the injection if you have:**

- severe lung, liver or heart problems.
- low numbers of red blood cells, platelets or white blood cells, as these might worsen during treatment
- bleeding problems and/or low number of platelets in your blood
- diarrhoea, constipation, nausea or vomiting, as this might worsen during treatment
- a history of fainting, dizziness or light-headedness in the past
- kidney problems
- liver problems
- numbness, tingling, or pain in the hands or feet (neuropathy) in the past, as it might worsen during treatment
- heart or blood pressure problems
- amyloidosis (as a result of abnormal deposit of amyloid (a protein) in various tissues in the body)
- shortness of breath or cough
- seizures
- Shingles (localised including around the eyes or spread across the body)

- symptoms of tumor 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. These may be signs of a serious brain infection and your doctor may suggest further testing and follow-up.
- mantle cell lymphoma and are given the medicine rituximab with BOTIGEN 3,5 you should tell your doctor.
- if you think you have 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.

**Children and Adolescents**

BOTIGEN 3,5 has not been studied in children or adolescents and therefore should not be used in this patient population.

**Other medicines and BOTIGEN 3,5**

Always tell your healthcare 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
- 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
- Ritonavir used to treat HIV infection

**BOTIGEN 3,5 with food and drink**

Refer to Section 3 (How BOTIGEN 3,5 is given).

**Pregnancy and breastfeeding**

This medicine may harm a baby developing in the womb. It is important not to become pregnant or father a child while you are having treatment with this medicine and for 3 months afterwards.
If you are pregnant or breastfeeding, think that you may be pregnant or are planning to have a baby, please consult your doctor, pharmacist or other healthcare provider for advice before you are given this medicine.

BOTIGEN 3,5 must not be used if you are pregnant or breastfeeding.
You must make sure that you do not become pregnant while receiving BOTIGEN 3,5. Both men and women must ensure adequate birth control measures are taken whilst receiving BOTIGEN 3,5, and for 3 months after treatment.

If you do become pregnant or are breastfeeding your baby while receiving BOTIGEN 3,5, please consult your doctor, pharmacist or other healthcare provider for advice.

If you wish to restart breastfeeding after BOTIGEN 3,5 treatment, you must discuss this with your doctor, pharmacist or other healthcare provider, who will tell you when it is safe to do so.

**Driving and using machines:**

It is not always possible to predict to what extend BOTIGEN 3,5 may interfere with 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 BOTIGEN 3,5 affects them.
BOTIGEN 3,5 might cause low blood pressure, tiredness, dizziness, fainting, or blurred vision.

Do not drive or operate tools or machines if you experience such side effects; even if you do not, you should still be cautious.

**BOTIGEN 3,5 contains mannitol (35 mg/5 mL)**

BOTIGE 3,5 contains mannitol. If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before being given this medicine.

**3. How BOTIGEN 3,5 is given**

You will not be expected to give yourself BOTIGEN 3,5. It will be given to you by a person who is qualified to do so.

The usual starting dose of BOTIGEN 3,5 is 1,3 mg/$m^2$ body surface area twice a week.

Your doctor will work out your dose of BOTIGEN 3,5 according to your height and weight (body surface area).

You will receive BOTIGEN 3,5 in a specialised medical unit, under the supervision of a doctor experienced in the use of cytotoxic medicines.

You will be given BOTIGEN 3,5 intravenously (in a vein) or subcutaneously (under the skin).

BOTIGEN 3,5 powder has to be dissolved before administration. This will be done by a healthcare provider. The resulting solution is then either injected into a vein or under the skin. Injection into the vein is rapid, taking 3 to 5 seconds. Injection under the skin is in either the thigh or the abdomen.

Your doctor will tell you how long your treatment with BOTIGEN 3,5 will last. 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 BOTIGEN 3,5 is given alone, you will receive 4 doses of BOTIGEN 3,5 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. At least 72 hours should elapse between consecutive doses of BOTIGEN 3,5. You might receive up to 8 cycles (24 weeks).

You may also be given BOTIGEN 3,5 together with the medicines pegylated liposomal doxorubicin or dexamethasone.

When BOTIGEN 3,5 is given together with pegylated liposomal doxorubicin, you will receive BOTIGEN 3,5 intravenously as a 21-day treatment cycle and pegylated liposomal doxorubicin 30 mg/m$^2$ is given on day 4 of the BOTIGEN 3,5, 21-day treatment cycle as an intravenous infusion after the BOTIGEN 3,5 intravenous injection. You might receive up to 8 cycles (24 weeks).

**Previously untreated multiple myeloma**

Patients with previously untreated multiple myeloma may also be given BOTIGEN 3,5 together with the 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, BOTIZEN 3,5 is administered twice weekly on days 1, 4, 8, 11, 22, 25, 29 and 32.
- In cycles 5 to 9, BOTIZEN 3,5 is administered once weekly on days 1, 8, 22 and 29.

Melphalan (9 mg/m$^2$) and prednisone (60 mg/m2) are both given orally on days 1, 2, 3 and 4 of the first week of each cycle.

If you have not been treated before for multiple myeloma, and you are suitable for blood stem cell transplantation you will receive BOTIGEN 3,5 intravenously together with the medicines dexamethasone, or dexamethasone and thalidomide, as induction treatment.

When BOTIGEN 3,5 is given together with dexamethasone, you will receive BOTIGEN 3,5 intravenously as a 21-day treatment cycle and dexamethasone 40 mg is given orally on days 1, 2, 3, 4, 8, 9, 10 and 11 of the BOTIGEN 3,5,21-day treatment cycle. You will receive 4 cycles (12 weeks).

When BOTIGEN 3,5 is given together with thalidomide and dexamethasone, the duration of a treatment cycle is 28 days (4 weeks).
Dexamethasone 40 mg is given orally on days 1, 2, 3, 4, 8, 9, 10 and 11 of the BOTIGEN 3,5, 28-day treatment cycle and thalidomide is given orally daily at 50 mg up to day 14 of the first cycle, and if tolerated the thalidomide dose is increased to 100 mg on days 15-28 and may be further increased to 200 mg daily from the second cycle onwards. You might receive up to 6 cycles (24 weeks).

**Progressive mantle cell lymphoma**

When BOTIGEN 3,5 is given alone, you will receive 4 doses of BOTIGEN 3,5 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 mantle cell lymphoma**

If you have not been treated before for mantle cell lymphoma you will receive BOTIGEN 3,5 intravenously together with the medicines rituximab, cyclophosphamide, doxorubicin and prednisone. BOTIGEN 3,5 is given intravenously on days 1, 4, 8 and 11, followed by a 'rest period' without treatment. The duration of a treatment cycle is 21-days (3 weeks). You might receive up to 8 cycles (24 weeks).
The following medicines are given on day 1 of each BOTIGEN 3,5 21-day treatment cycle as intravenous infusions:
Rituximab at 375 mg/$m^2$, cyclophosphamide at 750 mg/$m^2$ and doxorubicin at 50 mg/$m^2$
Prednisone is given orally at 100 mg/$m^2$ on days 1, 2, 3, 4 and 5 of the BOTIGEN 3,5 treatment cycle

**If you received too much BOTIGEN 3,5**

Since a healthcare provider will administer this medicine, he/she will control the dosage.

However in the event of overdosage your doctor will manage the overdosage.

**If you missed a dose of BOTIGEN 3,5:**

Since a health care provider will administer BOTIGEN 3,5, it is unlikely that the dose will be missed.

**4. POSSIBLE SIDE EFFECTS**

BOTIGEN 3,5 can have side effects.

Not all side effects reported for BOTIGEN 3,5 are included in this leaflet. Should your general health worsen or if you experience any untoward effects while given BOTIGEN 3,5, please consult your health care provider for advice.

If any of the following happens stop using BOTIGEN 3,5 and tell your doctor immediately or go to the casualty department at your nearest hospital:

- Swelling of the hands, feet ankles, face, lips and mouth or throat, which may cause difficulty in swallowing or breathing
- Peeling and blistering of the skin, mouth, eyes and genitals
- Rash or itching affecting your whole body
- Fainting

These are all very serious side effects. If you have them, you may have had a serious allergic reaction to BOTIGEN 3,5. You may need urgent medical attention or hospitalisation.

If you are given BOTIGEN 3,5, tell your doctor immediately or go to the casualty department of your nearest hospital if you notice any of the following:

- muscle cramping
- muscle weakness

- tingling, burning, pain, and loss of feeling in your hands and
- feet, any of which can be severe.
- confusion
- visual loss or disturbances
- blindness
- seizures
- headaches
- shortness of breath
- swelling of your feet or changes in your heartbeat
- high or low blood pressure
- tiredness
- fainting
- dizziness
- wheezing, coughing and breathing difficulties or tightness in the chest.
- chest pressure or pain
- yellow discoloration of the eyes and skin (jaundice) and changes in liver enzymes measured in blood tests.

These are all serious side-effects. You may need medical attention. Treatment with BOTIGEN 3,5 can frequently 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 BOTIGEN 3,5, 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.

The following side-effects have been reported, tell your doctor if you notice any of the following:

*Frequent:*

- Herpes zoster infection (including disseminated).
- Pneumonia, bronchitis, infection of the sinus passages.
- Reduction in the number of red blood cells and or white blood cells (see above).
- Dehydration and loss of appetite
- Changes in potassium in your blood, too much sugar in your blood.
- Depression which may be severe, confusion
- Difficulty in sleeping, sweating, anxiety.
- Sensitivity, numbness, tingling or burning sensation of the skin, or pain in the hands or feet, due to nerve damage.
- Fever, shivering fits.
- Blurred vision, eye pain
- General ill feeling, dizziness, light-headedness, or a feeling of weakness.
- Sudden fall of blood pressure on standing which may lead to fainting, high blood pressure, infection or swelling of a vein or tissue
- Chest pains or coughing with phlegm, shortness of breath with exercise.
- Difficulty in breathing, nose bleeds, cough, runny nose
- Heartburn, bloating, belching, wind or stomach pain, hiccups
- A sore mouth or lip, dry mouth, mouth ulcers or throat pain.
- Constipation with or without bloating (can be severe), abdominal pain
- Feeling sick (nausea) or vomiting, loss of appetite.
- Diarrhoea: if this happens, it is important that you drink more water than usual. Your doctor may give you another medicine to control diarrhoea.
- Rash

- Different types of rash and/or itching, lumps on the skin or dry skin.
- Muscle pain or weakness, tiredness, headache.
- Muscle cramps, bone pain, pain in your limbs or back.
- Kidney problems and painful or difficult urination
- Fatigue, fever, weakness, flu-like symptoms, swelling, chest pain
- Weight loss, loss of taste.
- Shortness of breath without exercise.
- Overtiredness (fatigue).
- Redness of the skin or redness and pain at the injection site.
- Infection of the outermost layer of the eye and inner surface of the eyelids (conjunctivitis)

*Less frequent:*

- General infections and infections of e.g. lungs, respiratory track, kidney and bladder, intestines, mouth, eyes caused by bacteria or fungus
- Low blood counts of white and red blood cells and platelets
- swollen or enlarged lymph nodes
- Swelling of your lymph nodes.
- Tumor lysis syndrome with symptoms such as nausea, vomiting, diarrhoea, muscle cramps or twitches, weakness, numbness or tingling, fatigue, decreased urination
- Allergic reactions.
- Hormone abnormality affecting salt and water absorption.
- Changes in calcium, sodium, magnesium, uric acid, lower Vit $B_{12}$, and phosphates in your blood, too little sugar in your blood
- Loss of attention, restlessness or agitation, changes in your mental status, mood swings, sleep disorders
- Paralysis, seizures, migraine, restless legs, speech disorder

- 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.
- Hearing loss, deafness or ringing in the ears.
- 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.
- Facial blushing, hot flushes or tiny broken capillaries.
- 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.
- Bleeding from your bowels or stomach, bloody stools, bleeding in the brain, bleeding from the liver or bleeding from mucosal membranes e.g. mouth.
- Breathing becomes shallow, difficult or stops, wheezing, and difficulty in breathing, asthma, cough that produces frothy sputum that may be tinged with blood or coughing blood.
- Yellow discolouration of eyes and skin (jaundice).
- Mouth pain, retching.
- Abdominal pain.
- Poor movement in the intestines (including blockages).
- 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).
- Nail and skin disorders, such as hair loss
- Joint or muscle stiffness, muscle spasms or twitching, pain in
- jaw or your bottom, joint swelling and swelling
- Kidney problems such as an increased or decreased urine production (due to kidney damage), painful passing of urine or blood/proteins in the urine.
- Reversible Posterior Leukoencephalopathy Syndrome
- (RPLS), a severe reversible brain condition which includes

seizures, high blood pressure, headaches, tiredness,

confusion, blindness or other vision problems.

- 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.
- Poor circulation
- Problems with blood clotting
- Swelling of the lining around your heart or fluid around your heart
- Cerebrovascular disorders
- Arthritis, including welling 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, shortness of breath, shortness of breath without exercise, breathing that becomes shallow, difficult or stops, wheezing
- Overactive thyroid gland
- Inability to produce enough insulin or resistance to normal levels of insulin
- Infections or swelling of the mouth, mouth ulcers, oesophagus, stomach and intestines, sometimes associated with pain or bleeing, poor movement of the intestines (including blockage), abdominal or oesophageal discomfort, difficulty swallowing, vomiting of blood.
- Skin infections
- Tooth infections
- Swelling of the pancreas, blockage of the bile duct
- Genital pain, problem having an erection
- Weight increase
- Thirst
- Injection site or injection device related disorders
- Bruises, falls and injuries
- Swelling 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

- Benign (non-cancerous) cysts
- Heart probleems to include heart attack, angina
- Flushing
- Discolouration of the veins
- Swelling of the spinal nerve
- Problems with your ear, bleeding from your ear
- Underactivity of your thyroid gland
- Budd–Chiari syndrome (the clinical symptoms caused by blockage of the hepatic veins)
- Changes in or abnormal bowel function
- Breast disorders
- Vaginal tears
- Genital swelling
- Inability to tolerate alcohol consumption
- Wasting, or loss of body mass
- Increased appetite
- Fistula (abnormal connection between two spaces)
- Joint effusion
- Cysts in the lining of joints (synovial cysts)
- Fracture
- Breakdown of muscle fibers leading to other complications
- Cancer of the kidney
- Psoriasis like skin condition
- Cancer of the skin
- Increase of platelets or plasma cells (a type of white cell) in the blood
- Blood clot in small blood vessels (thrombotic microangiopathy)
- Abnormal reaction to blood transfusions
- Decreased sex drive

- Drooling
- Bulging eyes
- Rapid breathing
- Rectal pain
- Gallstones
- Hernia
- Injuries
- Brittle or weak nails
- Abnormal protein deposits in your vital organs
- Coma
- Intestinal ulcers
- Multi-organ failure
- Death

If you are given BOTIGEN 3,5 together with the other medicines for the treatment of mantle cell lymphoma the side effects you may get are listed below and tell your doctor if you notice any of the following:

*Frequent side effects:*

- Pneumonia
- Loss of appetite
- Sensitivity, numbness, tingling or burning sensation of the skin, or pain in the hands or feet, due to nerve damage
- Nausea and vomiting
- Diarrhoea
- Mouth ulcers
- Constipation
- Muscle pain, bone pain

- Hair loss and abnormal hair texture
- Tiredness, feeling weak
- Fever
- Shingles (localised including around the eyes or spread across the body)
- Herpes virus infections (Epstein-Barr virus infection)
- Bacterial and viral infections
- Respiratory infections, bronchitis, coughing with phlegm, flu like illness
- Fungal infections
- Inability to produce enough insulin or resistance to normal
- levels of insulin
- Fluid retention
- Difficulty or problems in sleeping
- Loss of consciousness
- Altered level of consciousness, confusion
- Feeling dizzy
- Increased heartbeat, high blood pressure, sweating,
- Abnormal vision, blurred vision
- Heart failure, heart attack, chest pain, chest discomfort, increased or reduced heart rate
- High or low blood pressure
- Sudden fall of blood pressure upon standing which may lead to fainting
- Shortness of breath with exercise
- Cough
- Hiccups
- Ringing in the ears, ear discomfort
- Bleeding from your bowels or stomach
- Heartburn
- Stomach pain, bloating

- Difficulty swallowing
- Infection or inflammation of the stomach and intestines
- Stomach pain
- Sore mouth or lip, throat pain
- Alteration of liver function
- Itching of skin
- Redness of skin
- Rash
- Muscle spasms
- Infection of the urinary tract
- Pain in limbs
- Swelling of body, to include eyes and other parts of the body
- Shivering
- Redness and pain at injection site
- General ill feeling
- Weight loss
- Weight increase

*Less frequent side effects*

- Hepatitis (swelling of the liver)
- Severe allergic reaction
- Movement disorders, paralysis, twitching
- Vertigo
- Hearing loss, deafness
- 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
- Blood clots in your lungs

- Yellow discoloration of the eyes and skin (jaundice)
- Lump in the eyelid (chalazion), red and swollen eyelids
- Blood clot in small blood vessels (thrombotic microangiopathy)
- Inflammation (swelling) of the protective membranes covering the brain and spinal cord (meningitis)
- Itching, burning or tenderness in the genital area (genital virus)
- Inflammation of the tonsils
- Pain in a nerve pathway (neuralgia)

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 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 BOTIGEN 3,5.

**5. HOW TO STORE BOTIGEN 3,5**

BOTIGEN 3,5 will be stored in the pharmacy.

Store all medicines out of reach of children.

Do not use this medicine after the expiry date stated on the vial and

the carton after EXP:

Before reconstitution:

Store at or below 25 °C.

Keep the vial in the outer carton in order to protect from light.

Reconstituted solutions:

The reconstituted solution should be used immediately after preparation. If the reconstituted solution is not used immediately, in-use storage times and conditions prior to use are the responsibility of the user. However, the reconstituted solution is stable for 8 hours at 25 °C stored in the original vial and/or a syringe, with a total storage time for the reconstituted medicine not exceeding 8 hours prior to administration. BOTIGEN 3,5 is for single use only. Discard any unused portion as per current requirements.

## 6. CONTENTS OF THE PACK AND OTHER INFORMATION

### What BOTIGEN contains

The active substance is: bortezomib

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

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

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

The other ingredients are: mannitol (35 mg per vial)

### What BOTIGEN 3,5 looks like and the contents of the pack

BOTIGEN 3,5 is supplied as a white to off white lyophilized cake or powder in a 10 ml Type 1 tubular colourless glass vial with a grey bromobutyl rubber stopper, sealed with a light green flip off aluminium seal.

The vial is contained in a transparent blister pack consisting of a tray with a lid.

Each pack contains 1 single-use vial.

**Holder of Certificate of Registration**

Ranbaxy Pharmaceuticals (Pty) Ltd

14 Lautre Road,

Stormill, Ext.1, Roodepoort, 1724

South Africa

P.O. Box 43486

Industria, 2042

This leaflet was last revised in

27 January 2025

**Registration number**

51/26/0163

**Pasiëntinligtingsblad**

**SKEDULERINGSTATUS: S4**

**BOTIGEN 3,5** (Poeier vir oplossing vir inspuiting)

**Bortesomib** 3,5 mg (as 'n mannitol-boroniese ester) /flessie

Bevat suiker (35 mg mannitol per flessie)

**Lees hierdie hele inligtingsblad noukeurig deur voordat BOTIGEN 3,5 aan jou toegedien word:**

- Hou hierdie inligtingsblad. Dit mag nodig wees dat jy dit weer lees.
- Vra asseblief jou dokter, apteker, verpleegkundige of ander gesondheidsorgverskaffer indien jy verdere vrae het.
- **BOTIGEN 3,5** is vir jou persoonlik voorgeskryf en jy moenie jou medisyne met enige ander persoon deel nie. Dit kan skadelik vir hulle wees, selfs as hulle simptome dieselfde as joune is.

**Wat is in hierdie inligtingsblad**

1. Wat BOTIGEN 3,5 is en waarvoor dit gebruik word
2. Wat jy moet weet voordat BOTIGEN 3,5 aan jou toegedien word
3. Hoe BOTIGEN 3,5 toegedien word
4. Moontlike newe-effekte
5. Hoe om BOTIGEN 3,5 te bewaar
6. Inhoud van die verpakking en ander inligting

## 1. Wat BOTIGEN 3,5 is en waarvoor dit gebruik word

**BOTIGEN 3,5** bevat bortesomib as die aktiewe bestanddeel en behoort aan ‘n groep medisyne wat sitostatiese middels genoem word. Dit word gebruik om kankerselle dood te maak.

**BOTIGEN 3,5** word gebruik vir die behandeling van:

Veelvuldige miëloom (‘n kanker van die beenmurg) by volwassenes:

- In kombinasie met ander medisyne (melfalan en prednisoon), by pasiënte wat nie voorheen behandel is nie en nie geskik is vir hoë-dosis chemoterapie met bloed-stamseloorplanting nie
- Alleen of saam met ander medisyne, gepegileerde liposomale doksorubisien of deksametasoon, by pasiënte wie se siekte vererger (progressief) nadat ten minste een vooraf-behandeling ontvang is en vir wie bloed-stamseloorplanting nie suksesvol of geskik was nie.
- In kombinasie met die medisyne, deksametasoon of deksametasoon saam met talidomied, by pasiënte wie se siekte nie voorheen behandel is nie en voordat hoë-dosis chemoterapie met bloed-stamseloorplanting (induksie-behandeling) ontvang word.

Mantelsel-limfoom (‘n bloedkanker in die limfkliere) by volwassenes:

- Wie se siekte vererger (progressief) nadat ten minste een vooraf-behandeling ontvang is, een waarvan die medisyne antrasiklien (of mitosantroon) en/of rituksimab as deel van hulle chemoterapie-behandeling ingesluit behoort te gewees het.
- In kombinasie met die medisyne, rituksimab, siklofosfamied, doksorubisien en prednisoon, by pasiënte wie se siekte nie voorheen behandel is nie en vir wie bloed-stamseloorplanting nie geskik is nie.

## 2. Wat jy moet weet voordat BOTIGEN 3,5 aan jou toegedien word

**BOTIGEN 3,5 moenie aan jou toegedien word nie:**

- Indien jy hipersensitief (allergies) is vir bortesomib of vir enige van die ander bestanddele van BOTIGEN 3,5.
- Indien jy hipersensitief (allergies) is vir mannitol of boor.
- Indien jy sekere ernstige long- of hartprobleme het.

**Waarskuwings en voorsorgmaatreëls**

**Lig jou dokter of gesondheidsorgverskaffer in voordat die inspuiting aan jou toegedien word as jy die volgende het:**

- ernstige long-, lewer- of hartprobleme.
- lae telling van rooibloedselle, plaatjies of witbloedselle, aangesien hierdie kan vererger tydens behandeling
- bloedingsprobleme en/of lae telling van plaatjies in jou bloed
- diarree, hardlywigheid, naarheid of braking, aangesien dit kan vererger tydens behandeling
- ‘n geskiedenis van floute, duiseligheid of lighoofdigheid in die verlede gehad het
- nierprobleme
- lewerprobleme
- gevoelloosheid, tinteling of pyn in die hande of voete (neuropatie) in die verlede ervaar het, aangesien dit tydens behandeling kan vererger
- hart- of bloeddrukprobleme
- amiloïedose (as gevolg van abnormale neerslag van amiloïed (‘n proteïen) in verskeie weefsel in die liggaam)
- kortasemigheid of hoes

- toevalle
- gordelroos (gelokaliseerd, insluitend rondom die oë of versprei oor die hele liggaam)
- simptome van tumorlise-sindroom soos spierkrampe, spierswakheid, verwarring, visuele verlies of versteurings en kortasemigheid
- geheueverlies, sukkel om te dink, sukkel om te loop of verlies van visie. Hierdie kan tekens wees van ‘n ernstige breininfeksie en jou dokter kan verdere toetsing en opvolg voorstel.
- mantelsel-limfoom en as die middel rituksimab saam met **BOTIGEN 3,5** gegee word, moet jy jou dokter inlig.
- as jy vermoed dat jy nou hepatitis-B-infeksie het of in die verlede gehad het. In ‘n paar gevalle mag pasiënte wat hepatitis-B gehad ‘n hehaalde aanval van hepatitis kry wat noodlottig kan wees. Indien jy ‘n geskiedenis van hepatitis-B-infeksie het, sal jy noukeurig deur jou dokter dopgehou word vir tekens van aktiewe hepatitis-B.

**Kinders en adolessente**

**BOTIGEN 3,5** is nie in kinders of adolessente bestudeer nie en moet daarom nie by hierdie pasiëntpopulasie gebruik word nie.

**Ander medisyne en BOTIGEN 3,5**

Lig jou gesondheidsorgverskaffer altyd in indien jy enige ander medisyne neem. (Dit sluit komplementêre of tradisionele medisyne in.)

Lig jou dokter in as jy medisyne gebruik wat enige van die volgende aktiewe bestanddele bevat:

- Ketokonasool – gebruik om swaminfeksie te behandel;
- Ritonavir – gebruik om MIV-infeksie te behandel;

- Rifampisien, ‘n antibiotikum wat gebruik word om bakteriële infeksie te behandel;
- Karbamasepien, fenitoïen of fenobarbitoon – gebruik om epilepsie te behandel;
- Johanneskruid (*Hypericum perforatum*) – gebruik vir depressie of ander toestande;
- Orale antidiabetiese middels;

**BOTIGEN 3,5 saam met voedsel of drinkgoed**

Verwys na afdeling 3 (Hoe BOTIGEN 3,5 toegedien word).

**Swangerskap en borsvoeding**

Hierdie medisyne kan ‘n baba, wat in die baarmoeder ontwikkel, skade aandoen. Dit is belangrik om nie swanger te raak of ‘n vader te wees vir ‘n kind terwyl jy onder behandeling met hierdie medisyne is en vir 3 maande daarna nie. Indien jy swanger is, vermoed dat jy swanger mag wees of as jy beplan om swanger te raak, moet jy asseblief jou dokter, apteker of ander gesondheidsorgverskaffer raadpleeg vir advies voordat hierdie medisyne aan jou toegedien word.

**BOTIGEN 3,5** moenie gebruik word as jy swanger is of jou baba borsvoed nie.
Jy moet seker maak dat jy nie swanger raak terwyl jy **BOTIGEN 3,5** ontvang nie**.** Beide mans en vroue moet verseker dat hulle voldoende geboortebeperkingsmaatreëls toepas terwyl hulle **BOTIGEN 3,5** ontvang, en vir 3 maande ná behandeling.

Indien jy swanger raak of jou baba borsvoed terwyl jy **BOTIGEN 3,5** ontvang, moet jy asseblief jou dokter, apteker of ander gesondheidsorgverskaffer raadpleeg vir advies.

Indien jy graag borsvoeding wil hervat ná behandeling met **BOTIGEN 3,5**, moet jy dit met jou dokter, apteker of ander gesondheidsorgverskaffer bespreek. Hulle sal jou inlig wanneer dit veilig is om dit te doen.

**Bestuur en gebruik van masjinerie:**

Dit is nie altyd moontlik om te voorspel tot watter mate **BOTIGEN 3,5** met die daaglikse aktiwiteite van ‘n pasiënt sal inmeng nie. Pasiënte moet seker maak dat hulle nie betrokke raak in die bogenoemde aktiwiteite totdat hulle bewus is tot watter mate **BOTIGEN 3,5** hulle sal affekteer nie.

**BOTIGEN 3,5** kan lae bloeddruk, moegheid, duiseligheid, floute of belemmerde visie veroorsaak.

Moenie bestuur of apparaat of masjinerie hanteer as jy sulke newe-effekte ondervind nie; selfs as jy dit nie ondervind het nie, moet jy steeds versigtig wees.

**BOTIGEN 3,5 bevat mannitol (35 mg/5 mL)**

**BOTIGEN 3,5** bevat mannitol. As jy deur jou dokter ingelig is dat jy ‘n onverdraagsaamheid teenoor sekere suikers het, moet jy jou dokter raadpleeg voordat hierdie medisyne aan jou toegedien word.

**3. Hoe BOTIGEN 3,5 toegedien word**

Daar sal nie van jou verwag word om **BOTIGEN 3,5** aan jouself toe te dien nie. Dit sal aan jou toegedien word deur ‘n persoon wat gekwalifiseer is om dit te doen.

Die normale aanvangsdosis van **BOTIGEN 3,5** is 1,3 mg/m$^2$ liggaamsoppervlakte twee keer per week. Jou dokter sal jou dosis van **BOTIGEN 3,5** uitwerk volgens jou lengte en gewig (liggaamsoppervlakte).

Jy sal **BOTIGEN 3,5** in ‘n gespesialiseerde mediese eenheid onder die toesig van ‘n dokter ontvang wat ervare is in die gebruik van sitotoksiese medisyne.

**BOTIGEN 3,5** sal intraveneus (binne-in ‘n aar) of subkutaan (onder die vel) aan jou toegedien word. **BOTIGEN 3,5** poeier moet opgelos word voor toediening. Dit sal deur ‘n gesondheidsorgverskaffer gedoen word. Die gevolglike oplossing word dan óf binne-in ‘n aar óf onder die vel ingespuit. Inspuiting binne-in die aar is vinnig, dit neem ongeveer 3 tot 5 sekondes. Inspuiting onder die vel is óf in die dy óf die maag.

Jou dokter sal jou inlig oor hoe lank jou behandeling met **BOTIGEN 3,5** sal duur. Jou dokter mag die dosis en totale aantal behandelingsiklusse verander, afhangende van hoe jy op die behandeling gereageer het, op die voorkoms van sekere newe-effekte en op jou onderliggende siektetoestande (bv. lewerprobleme).

Progressiewe veelvuldige miëloom

Wanneer slegs **BOTIGEN 3,5** toegedien word, sal jy 4 dosisse **BOTIGEN 3,5** intraveneus ontvang op dag 1, 4, 8 en 11, gevolg deur ‘n 10-dag ‘rusperiode’ sonder behandeling. Hierdie 21-dag periode (3 weke) is gelyk aan een behandelingsiklus. Ten minste 72 uur moet verloop tussen opeenvolgende dosisse van **BOTIGEN 3,5**. Jy kan tot 8 siklusse ontvang (24 weke).

**BOTIGEN 3,5** kan ook saam met die medisyne, pegileerde liposomale doksorubisien of deksametasoon aan jou toegedien word.

Wanneer **BOTIGEN 3,5** saam met pegileerde liposomale doksorubisien toegedien word, sal jy **BOTIGEN 3,5** intraveneus ontvang as ‘n 21-dag behandelingsiklus en gepegileerde liposomale doksorubisien 30 mg/m$^2$ sal op dag 4 van die **BOTIGEN 3,5**, 21-dag

behandelingsiklus as ‘n intraveneuse infusie ná die **BOTIGEN 3,5** intraveneuse inspuiting toegedien word. Jy mag tot 8 siklusse ontvang (24 weke).

**Vooraf-onbehandelde veelvuldige miëloom**

Aan pasiënte met vooraf-onbehandelde veelvuldige miëloom kan **BOTIGEN 3,5** ook saam met die medisyne, melfalan en prednisoon, toegedien word.

Die behandelingsiklus in hierdie geval is 42 dae (6 weke). Jy sal 9 siklusse ontvang (54 weke).

- In siklusse 1 tot 4, word **BOTIZEN 3,5** twee keer per week toegedien op dag 1, 4, 8, 11, 22, 25, 29 en 32.
- In siklusse 5 tot 9, word **BOTIZEN 3,5** een keer per week toegedien op dag 1, 8, 22 en 29.

  Melfalan (9 mg/m$^2$) en prednisoon (60 mg/m$^2$) word albei oraal toegedien op dag 1, 2, 3 en 4 van die eerste week van elke siklus.

  Indien jy nie voorheen vir veelvuldige miëloom behandel is nie en jy geskik is vir bloed-stamseloorplanting, sal jy **BOTIGEN 3,5** intraveneus saam met die medisyne, deksametasoon of deksametasoon en talidomied, ontvang, as induksie-behandeling.

Wanneer **BOTIGEN 3,5** saam met deksametasoon toegedien word, sal jy **BOTIGEN 3,5** intraveneus as ‘n 21-dag behandelingsiklus ontvang en 40 mg deksametasoon sal oraal op dag 1, 2, 3, 4, 8, 9, 10 en 11 van die **BOTIGEN 3,5** 21-dag behandelingsiklus, toegedien word. Jy sal 4 siklusse ontvang (12 weke).

Wanneer **BOTIGEN 3,5** saam met talidomied en deksametasoon toegedien word, is die duur van die behandelingsiklus 28 dae (4 weke).

40 mg Deksametasoon word oraal toegedien op dag 1, 2, 3, 4, 8, 9, 10 en 11 van die **BOTIGEN 3,5**, 28-dag behandelingsiklus en talidomied word daagliks oraal toegedien teen 50 mg tot op dag 14 van die eerste siklus, en as die dosis verdra word, word die talidomieddosis verhoog tot 100 mg op dag 15-28 en mag dit voortaan verder verhoog word tot 200 mg daagliks vanaf die tweede siklus. Jy kan tot 6 siklusse ontvang (24 weke).

**Progressiewe mantelsellimfoom**

Wanneer slegs **BOTIGEN 3,5** toegedien word, sal jy 4 dosisse **BOTIGEN 3,5** intraveneus ontvang op dag 1, 4, 8 en 11, gevolg deur ‘n 10-dag ‘rusperiode’ sonder behandeling. Hierdie 21-dag periode (3 weke) is gelyk aan een behandelingsiklus. Jy kan tot 8 siklusse ontvang (24 weke).

**Vooraf-onbehandelde mantelsellimfoom**

As jy nie voorheen vir mantelsellimfoom behandel is nie, sal jy **BOTIGEN 3,5** intraveneus saam met die medisyne, rituksimab, siklofosfamied, doksorubisien en prednisoon ontvang. **BOTIGEN 3,5** word intraveneus op dag 1, 4, 8 en 11 toegedien, gevolg deur ‘n ‘rusperiode’ sonder behandeling. Die duur van ‘n behandelingsiklus is 21-dae (3 weke). Jy kan tot 8 siklusse ontvang (24 weke).

Die volgende medisyne word op dag 1 of elke **BOTIGEN 3,5** 21-dag behandelingsiklus as intraveneuse infusie toegedien:

Rituksimab teen 375 mg/m$^2$, siklofosfamied teen 750 mg/m$^2$ en doksorubisien teen 50 mg/m$^2$

Prednisoon word oraal toegedien teen 100 mg/m$^2$ op dag 1, 2, 3, 4 en 5 van die **BOTIGEN 3,5** behandelingsiklus

**As jy te veel BOTIGEN 3,5 ontvang het:**

Aangesien ’n gesondheidsorgverskaffer **BOTIGEN 3,5** sal toedien, sal hy/sy die dosis beheer. In geval van oordosering, sal jou dokter egter die oordosering bestuur.

**As jy ‘n dosis van BOTIGEN 3,5 oorgeslaan het:**

Aangesien ’n gesondheidsorgverskaffer **BOTIGEN 3,5** sal toedien, is dit onwaarskynlik dat die dosis oorgeslaan sal word.

## 4. MOONTLIKE NEWE-EFFEKTE

BOTIGEN 3,5 kan newe-effekte hê.

Nie alle newe-effekte wat vir **BOTIGEN 3,5** aangemeld word, is in hierdie inligtingsblad ingesluit nie. Indien jou algemene gesondheid verswak of indien jy enige ongunstige effekte ondervind terwyl jy **BOTIGEN 3,5** ontvang, raadpleeg asseblief jou gesondheidsorgverskaffer vir advies.

Indien enige van die volgende simptome voorkom, hou op om **BOTIGEN 3,5** te ontvang en sê dadelik vir jou dokter of gaan na die noodgevalle-afdeling by jou naaste hospitaal:

- Swelling van jou hande, voete, enkels, gesig, lippe, mond of keel, wat probleme met sluk of asemhaling kan veroorsaak
- Afskilfering of blasievorming op die vel, mond, oë en geslagsdele
- Uitslag of gejeuk wat jou hele liggaam raak
- Floute

Hierdie is almal baie ernstige newe-effekte. Jy mag ’n ernstige allergiese reaksie teen **BOTIGEN 3,5** gehad het as jy dit het. Jy mag dringend mediese bystand of hospitalisasie benodig.

As **BOTIGEN 3,5** aan jou toegedien word, sê dadelik vir jou dokter of gaan na die noodvalle-afdeling by jou naaste hospitaal indien jy enige van die volgende opmerk:

- spierkrampe
- spierswakheid
- tintelende, brandende pyn en verlies aan gevoel in jou hande en voete, waarvan enige van hierdie ernstig kan wees
- verwarring
- visuele verlies of versteurings
- blindheid
- toevalle
- hoofpyn
- kortasemigheid
- swelling van jou voete of veranderinge in jou hartklop
- hoë of lae bloeddruk
- moegheid
- floute
- duiseligheid
- hyging, hoes en asemhalingsprobleme of benoudheid in die borskas
- drukking of pyn in die borskas
- geelverkleuring van die oë en vel (geelsug) en veranderinge in lewerensieme wat in bloedtoetse waargeneem word.

Hierdie is almal ernstige newe-effekte. Jy mag dringend mediese bystand nodig hê.

Behandeling met **BOTIGEN 3,5** kan dikwels ‘n afname in die aantal rooi- en witbloedselle en plaatjies in jou bloed veroorsaak. Jy moet daarom gereelde bloedtoetse vóór en tydens behandeling met **BOTIGEN 3,5** ondergaan om jou bloedseltelling te kontroleer.

Jy kan ‘n afname ervaar in die aantal:

- plaatjies, wat jou meer geneig sal maak vir kneusing of vir bloeding sonder enige duidelike besering (bv., bloeding van jou ingewande, maag, mond en tandvleise of bloeding in die brein of bloeding van die lewer)
- rooibloedselle, wat anemie kan veroorsaak met simptome soos moegheid en bleekheid
- witbloedselle wat kan veroorsaak dat jy meer geneig is om infeksie te kry of griepagtige simptome.

Die volgende newe-effekte is aangemeld; lig jou dokter in as jy enige van die volgende opmerk:

*Dikwels:*

- Herpes zoster-infeksie (insluitend verspreide infeksie).
- Longontsteking, brongitis, infeksie van die sinusholtes.
- Vermindering in die aantal rooibloedselle en/of witbloedselle (sien hierbo).
- Ontwatering en verlies aan eetlus.
- Veranderinge in kaliumvlakke in jou bloed, te veel suiker in jou bloed.
- Depressie wat ernstig kan wees, verwarring.
- Sukkel om te slaap, sweet, angstigheid.
- Sensitiwiteit, gevoelloosheid, tintelende of brandende sensasie van die vel of pyn in die hande of voete as gevolg van senuweeskade.
- Koors, bewerigheid, toevalle.
- Belemmerde visie, oogpyn
- Algemene onwel gevoel, duisligheid, lighoofdigheid of ‘n gevoel van swakheid.
- Skielike daling in die bloeddruk wanneer jy opstaan, wat kan lei tot floute, hoë bloeddruk, infeksie of swelling van ‘n aar of weefsel
- Borskaspyne of hoes met slym, kortasemigheid met oefening.

- Moeilike asemhaling, neusbloedings, hoes, loopneus
- Sooibrand, opgeblasenheid, breek winde op, winde of maagpyn, hik
- ‘n Seer mond of lip, droë mond, mondsere of keelpyn.
- Hardlywigheid, met of sonder opgebalsenheid (kan ernstig wees), buikpyn
- Mislike gevoel (naarheid) of braking, verlies aan eetlus.
- Diarree: indien dit gebeur, is dit belangrik dat jy meer water as gewoonlik sal drink. Jou dokter kan ‘n ander medisyne vir jou voorskryf om die diarree te beheer.
- Uitslag. Verskillende soorte uitslag en/of gejeuk, knoppe op die vel of droë vel.
- Spierpyn of swakheid, moegheid, hoofpyn.
- Spierkrampe, beenpyn, pyn in jou ledemate of rug.
- Nierprobleme en pynlike of moeilike urinering.
- Moegheid, koors, swakheid, griepagtige simptome, swelling, borskaspyn.
- Gewigsverlies, smaakverlies.
- Kortasemigheid sonder oefening.
- Oormoegheid (uitputting).
- Rooiheid van die vel of rooiheid en pyn by die inspuitplek.
- Infeksie van die heel buitenste laag van die oog en binneste oppervlak van die ooglede (konjunktivitis)

*Minder dikwels:*

- Algemene infeksie en infeksie van bv. longe, respiratoriese stelsel, nier en blaas, ingewande, mond, oë veroorsaak deur bakterieë of swamme.
- Lae bloedtellings van wit-en rooibloedselle en plaatjies.
- Geswelde en vergrote limfknope.
- Swelling van jou limfknope.

- Tumorlise-sindroom met simptome soos naarheid, braking, diarree, spierkrampe of -trekkings, swakheid, gevoelloosheid of tinteling, moegheid verminderde urinering.
- Allergiese reaksies.
- Hormoonabnormaliteite wat sout- en waterabsorpsie affekteer.
- Veranderinge in kalsium, natrium, magnesium, uriensuur, laer Vit $B_{12}$, en fosfate in jou bloed, te min suiker in jou bloed.
- Verlies aan aandag, rusteloosheid of agitasie, veranderinge in jou geestestoestand, gemoedsversteuring, slaapversteurings
- Verlamming, toevalle, migraine, rustelose bene, spraakversteuring
- Geïrriteerde oë, uitermatige nat of droë oë, afskeiding vanuit die oë, abnormale visie, ooginfeksie (insluitend herpes zoster), bloeding van die oog of sensitiwiteit vir lig.
- Skade aan die optiese senuwee en blindheid.
- Gehoorverlies, doofheid of suising in die ore.
- Hartkloppings (sensasie van vinnige of onreëlmatige hartklop), veranderinge in hartklop, hartversaking, hartaanval, borskaspyn, ongemak in die borskas of verlaagde vermoë van die werking van die hart.
- Blosing van die gesig, warm gloede of klein gebreekte bloedvaatjies.
- Inflammasie van die bloedvate wat as klein rooi of pers kolletjies (gewoonlik op die bene) tot kneusingagtige gedeeltes op die vel kan voorkom.
- Bloeding van jou ingewande of maag, bloederige stoelgange, bloeding in die brein, bloeding van die lewer of bloeding van slymvliesmembrane bv. die mond.
- Asemhaling word vlak, is moeilik of hou op, hyging, sukkel met asemhaling, asma, hoes wat skuimerige sputum voortbring wat gevlek kan wees met bloed of die ophoes van bloed.
- Geelverkleuring van die oë en vel (geelsug).

- Mondpyn, braking.
- Buikpyn.
- Swak ingewandsbeweging (insluitend blokkasies).
- Ernstige velreaksies, wat blase kan hê en die mond, keel, oë en geslagsdele aantas en wat lewensbedreigend kan wees (Stevens Johnson se sindroom en toksiese epidermale nekrolise).
- Nael- en velversteurings, soos haarverlies.
- Gewrig- of spierstyfheid, spierspasmas of trekkings, pyn in die kakebeen of jou agterstewe, gewrigspyn en swelling.
- Nierprobleme soos ‘n verhoogde of verlaagde produksie van urine (as gevolg van nierskade), pynlike passering van urine of bloed/proteïene in die urine.
- Omkeerbare Posterior Leuko-ensefalopatie-sindroom (RPLS), ‘n ernstige omkeerbare breintoestand wat toevalle, hoë bloeddruk, hoofpyn, moegheid, verwarring, blindheid of ander visuele probleme insluit.
- Progressiewe multifokale leuko-ensefalopatie, ‘n seldsame gewoonlik dodelike virale siektetoestand gekenmerk deur progressiewe skade of inflammasie van die witstof van die brein op veelvuldige plekke.
- Swak sirkulasie.
- Probleme met bloedstolling.
- Swelling van die voering rondom jou hart of vloeistof rondom jou hart.
- Serebrovaskulêre versteurings
- Artritis, insluitend swelling van die gewrigte in die vingers, tone en die kakebeen.
- Versteurings wat jou longe affekteer wat voorkom dat jou liggaam genoeg suurstof kry. Sommige van hierdie sluit moeilike asemhaling en kortasemigheid sonder oefening in sodat asemhaling vlak raak, moeilik raak of ophou, hyging.

- Ooraktiewe skildklier.
- Onvermoë om genoeg insulien te vervaardig of weerstand teen normale vlakke van insulien
- Infeksie of swelling van die mond, mondsere, esofagus, maag en ingewande, somtyds geassosieer met pyn of bloeding, swak dermbewegings (insluitend blokkasie), abdominale of esofageale ongemak, moeilike sluk, braking van bloed.
- Velinfeksie
- Tandinfeksie
- Swelling van die pankreas, blokkasie van die galbuis
- Pyn in geslagsdele, probleme om ‘n ereksie te verkry
- Gewigstoename
- Dors
- Inspuitplek- of inspuittoestel-verwante versteurings
- Kneusings, val en beserings
- Swelling of bloeding van die bloedvate wat as klein rooi of pers kolletjies (gewoonlik op die bene) tot groot kneusingagtige gedeeltes onder die vel of weefsel kan voorkom
- Goedaardige (nie-kankeragtige) siste
- Hartprobleme om hartaanval in te sluit, angina
- Blosing
- Verkleuring van die are
- Swelling van die spinale senuwee
- Probleme met jou oor, bloeding vanuit jou oor
- Onderaktiwiteit van jou skildklier
- Budd–Chiari-sindroom (die kliniese simptome word veroorsaak deur die blokkasie van die lewervate)

- Veranderinge in of abnormale dermfunksie
- Borsversteurings
- Vaginale skeure
- Swelling van die geslagsdele
- Onvermoë om alkoholgebruik te verdra
- Wegkwyning of verlies aan liggaamsmassa
- Verhoogde eetlus
- Fistels (abnormale verbinding tussen twee spasies)
- Gewrigseffusie
- Siste in die voering van gewrigte (sinoviale siste)
- Fraktuur
- Afbraak van spierweefsel wat tot ander komplikasies lei
- Kanker van die nier
- Psoriase-agtige veltoestand
- Kanker van die vel
- Verhoging van plaatjies of plasmaselle (‘n soort witsel) in die bloed
- Bloedklont in klein bloedvate (trombotiese mikro-angiopatie)
- Abnormale reaksie op bloedoortappings
- Afname in seksdrang
- Kwyl
- Uitpeul oë
- Vinnige asemhaling
- Rektale pyn
- Galstene
- Breuk

- Beserings
- Bros of swak naels
- Abnormale proteïenneerslae in jou lewensbelangrike organe
- Koma
- Intestinale swere
- Multi-orgaanversaking
- Sterfte

Indien **BOTIGEN 3,5** saam met die ander medisyne vir die behandeling van mantelsellimfoom toegedien word, word die newe-effekte wat jy mag ondervind hieronder gelys. Lig jou dokter in as jy enige van die volgende opmerk:

*Dikwelse newe-effekte:*

- Longontsteking
- Verlies aan eetlus
- Sensitiwiteit, gevoelloosheid, tinteling of branderige sensasie op die vel, of pyn in die hande of voete as gevolg van senuweebeskadiging
- Naarheid en braking
- Diarree
- Mondsere
- Hardlywigheid
- Spierpyn, beenpyn
- Haarverlies en abnormale haartekstuur
- Moegheid, voel swak
- Koors
- Gordelroos (gelokaliseerd insluitend rondom die oë of oor die liggaam versprei)

- Herpes virus-infeksie (Epstein-Barr-virusinfeksie)
- Bakteriële en virale infeksie
- Respiratoriese infeksie, brongitis, hoes met slym, griepagtige simptome
- Swaminfeksie
- Onvermoë om genoeg insulien te produseer of weerstand teen normale vlakke van insulien
- Vogretensie
- Sukkel om te slaap of probleme met slaap
- Verlies van bewussyn
- Gewysigde vlak van bewussyn, verwarring
- Voel duiselig
- Vinniger hartklop, hoë bloeddruk, sweet,
- Abnormale visie, belemmerde visie
- Hartversaking, hartaanval, borskaspyn, ongemak in borskas, verhoogde of verlaagde hartritme
- Hoë of lae bloeddruk
- Skielike daling van bloeddruk wanneer opgestaan word en wat kan lei tot floute
- Kortasemigheid met oefening
- Hoes
- Hik
- Suising in die ore, oorongemak
- Bloeding vanaf jou ingewande of maag
- Sooibrand
- Maagpyn, opgeblasenheid
- Moeilike sluk

- Infeksie of inflammasie van die maag en ingewande
- Maagpyn
- Seer mond of lip, keelpyn
- Wysiging van lewerfunksie
- Jeukerige vel
- Rooiheid van die vel
- Uitslag
- Spierspasma
- Infeksie van die urienweg
- Pyn in die ledemate
- Swelling van die liggaam, insluitend oë en ander dele van die liggaam
- Bewerigheid
- Rooiheid en pyn by die inspuitplek
- Algemene onwel gevoel
- Gewigsverlies
- Gewigstoename

*Minder dikwelse newe-effekte:*

- Hepatitis (swelling van die lewer)
- Ernstige allergiese reaksie
- Bewegingsversteurings, verlamming, trekkings
- Vertigo
- Gehoorverlies, doofheid
- Versteurings wat jou longe affekteer wat voorkom dat jou liggaam voldoende suurstof ontvang. Sommige van hierdie sluit moeilike asemhaling en kortasemigheid sonder oefening in sodat asemhaling vlak raak, moeilik raak of ophou, hyging.

- Bloedklonte in jou longe
- Geelverkleuring van die oë en vel (geelsug)
- Knop in die ooglid (chalasion), rooi en geswelde ooglede
- Bloedklont in klein bloedvate (trombotiese mikro-angiopatie)
- Inflammasie (swelling) van die beskermende membrane wat die brein en spinaalkoord beskerm (meningitis)
- Jeukerigheid, branderigheid of teerheid in die genitale area (genitale virus)
- Inflammasie van die mangels
- Pyn in 'n senuweebaan (neuralgie)

Indien jy enige newe-effekte opmerk wat nie in hierdie inligtingsblad gelys word nie, lig asseblief jou dokter of apteker daarvan in.

**Aanmelding van newe-effekte**

Praat met jou dokter of apteker of verpleegkundige as jy newe-effekte ondervind. Jy kan ook newe-effekte by SAHPRA aanmeld *via* die "6.04 Adverse Drug Reaction Reporting Form", wat aanlyn beskikbaar is onder SAHPRA se publikasies:

https://www.sahpra.org.za/Publications/Index/8

Deur newe-effekte aan te meld, kan jy meer inligting oor die veiligheid van **BOTIGEN 3,5** verskaf.

## 5. HOE OM BOTIGEN 3,5 TE BEWAAR

**BOTIGEN 3,5** sal in die apteek bewaar word.

Bewaar alle medisyne buite die bereik van kinders.

Moenie hierdie medisyne ná die vervaldatum soos op die flessie en karton aangedui, gebruik nie.

Vóór hersamestelling:

Bewaar by of onder 25 °C.

Hou die flessie in die buitenste karton om dit teen lig te beskerm.

Hersaamgestelde oplossings:

Die hersaamgestelde oplossing moet onmiddellik ná voorbereiding gebruik word. Indien die hersaamgestelde oplossing nie onmiddellik gebruik word nie, is in-gebruiksbewaringstye en toestande voor gebruik, die verantwoordelikheid van die gebruiker. Die hersaamgestelde oplossing is egter stabiel vir 8 uur teen 25 °C as dit bewaar word in die oorspronklike flessie en/of ‘n spuit, met ‘n totale bewaringstyd vir die hersaamgestelde medisyne om nie 8 uur voor toediening te oorskry nie. **BOTIGEN 3,5** is slegs vir enkelgebruik. Gooi enige ongebruikte gedeelte weg volgens huidige vereistes.

## 6. INHOUD VAN DIE VERPAKKING EN ANDER INLIGTING

### Wat BOTIGEN bevat

Die aktiewe bestanddeel is: bortesomib

Elke flessie bevat 3,5 mg bortesomib (as ‘n mannitol-boroniese ester).

Ná hersamestelling, bevat elke 1 mL oplossing vir subkutane inspuiting 2,5 mg bortesomib.

Ná hersamestelling, bevat elke 1 mL oplossing vir intraveneuse inspuiting 1 mg bortesomib.

Die ander bestanddele is: mannitol (35 mg per flessie)

### Hoe BOTIGEN 3,5 lyk en inhoud van die verpakking

**BOTIGEN 3,5** word voorsien as ‘n wit tot naaswit gevriesdroogde koekie of poeier in ‘n 10 ml Tipe-1 buisvormige kleurlose glasflessie met ‘n grys bromobutiel-rubberprop, verseël met ‘n liggroen aftrekbare aluminiumseël.

Die flessie word verpak in ‘n deurskynende stulpverpakking bestaande uit ‘n bakkie met ‘n deksel. Elke pakkie bevat 1 flessie vir enkelgebruik.

**Houer van die registrasiesertifikaat**

Ranbaxy Pharmaceuticals (Pty) Ltd

Lautreweg 14,

Stormill, Uitbreiding 1, Roodepoort, 1724

Suid-Afrika

Posbus 43486

Industria, 2042

Hierdie inligtingsblad was laas hersien op

27 Januarie 2025

**Registrasienommer**

51/26/0163