

PROPOSED PATIENT INFORMATION LEAFLET

SCHEDULING STATUS: S4

BORTEZOMIB 3.5 MG EUROLAB 3,5 mg Powder for solution for injection

Bortezomib (as a mannitol boronic ester)

Read all of this leaflet carefully before you are given BORTEZOMIB 3.5 MG EUROLAB

- 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 BORTEZOMIB 3.5 MG EUROLAB is and what it is used for
2. What you need to know before you are given BORTEZOMIB 3.5 MG EUROLAB
3. How BORTEZOMIB 3.5 MG EUROLAB will be administered to you
4. Possible side effects
5. How to store BORTEZOMIB 3.5 MG EUROLAB
6. Contents of the pack and other information

1 What BORTEZOMIB 3.5 MG EUROLAB is and what it is used for

What BORTEZOMIB 3.5 MG EUROLAB is

BORTEZOMIB 3.5 MG EUROLAB contains the active substance 'bortezomib' which belongs to a group of medicines called proteasomes. Proteasomes play an important role in controlling cell function and growth. By interfering with their function, bortezomib can kill cancer cells.

What BORTEZOMIB 3.5 MG EUROLAB is used for

BORTEZOMIB 3.5 MG EUROLAB is used for the treatment of multiple myeloma (a cancer of the bone marrow) and mantle cell lymphoma (a blood cancer in the lymph glands) in patients older than 18 years. It may be used alone or in combination with other medicines.

2 What you need to know before you take BORTEZOMIB 3.5 MG EUROLAB

Do not take BORTEZOMIB 3.5 MG EUROLAB

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

Warnings and Precautions

Special care should be taken with BORTEZOMIB 3.5 MG EUROLAB:

- if you experience diarrhoea, constipation, nausea or vomiting
- if you have unexplained bleeding or bruising. Your doctor will conduct tests to monitor your blood counts
- if you develop painful, usually itchy rash as this may be shingles (localised including around the eyes or spread across the body)
- if you experience memory loss, trouble thinking, difficulty with walking, loss of vision, trouble speaking or muscle weakness. These may be signs of a serious brain infection and your doctor may suggest further testing and follow-up
- if you have numbness, tingling, or pain in the hands or feet (neuropathy)
- if you get seizures
- if you experience low blood pressure that happens when standing up from sitting or lying down
- if you have a history of fainting, dizziness or lightheadedness or a sudden temporary loss of consciousness
- if you have recurring diarrhoea or vomiting that may result in dehydration

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- if you have with symptoms such as seizures, high blood pressure, headache, tiredness, confusion, blindness, and other visual and neurological disturbances
- if you have heart problems and/or water retention
- if you experience shortness of breath, difficulty breathing or cough
- if you have kidney problems
- if you have fever, weakness, loss of appetite, nausea, vomiting, abdominal pain, dark urine, light-coloured stools, joint pain, and yellow colouring of skin and/or eyes, that can be signs of liver problems or complications
- if you experience symptoms of tumour lysis syndrome such as muscle cramping, muscle weakness, confusion
- if you experience a rash, redness, itching, joint pain, fever and swelling of lymph nodes
- if you pass foamy or pink urine

You will have to take regular blood tests before and during your treatment with BORTEZOMIB 3.5 MG EUROLAB, to check your blood cell counts.

If you have mantle cell lymphoma and are given the medicine rituximab with BORTEZOMIB 3.5 MG EUROLAB 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.

You must read the package leaflets of all medicines to be taken in combination with BORTEZOMIB 3.5 MG EUROLAB for information related to these medicines before starting treatment with BORTEZOMIB 3.5 MG EUROLAB.

Children and adolescents

BORTEZOMIB 3.5 MG EUROLAB is not recommended for use in children and adolescents under the age of 18 years, as it is not known how the medicine will affect them.

Other medicines and BORTEZOMIB 3.5 MG EUROLAB

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

In particular, tell your doctor or nurse if you are taking any of the following medicines, as BORTEZOMIB 3.5 MG EUROLAB might affect how these medicines work or vice versa:

- some antifungal medicines, such as ketoconazole
- ritonavir, used to treat HIV infection
- certain antibiotics (for example rifampicin, ciprofloxacin, enoxacin)
- carbamazepine, phenytoin or phenobarbital used to treat epilepsy
- St. John's Wort (*Hypericum perforatum*), used for depression or other conditions
- oral antidiabetics (if you are diabetic, your doctor might have to adjust the dose of your diabetic medicine while you are being treated with BORTEZOMIB 3.5 MG EUROLAB).
- medications that can cause peripheral neuropathy (weakness, numbness and pain from nerve damage, usually in the hands and feet). For example amiodarone (for the treatment of irregular heartbeat), antivirals, isoniazid (for the treatment of tuberculosis), nitrofurantoin (antibiotic for lower urinary tract infection) or statins (for lowering cholesterol)

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.

Contraception in males and females

Male patients treated with BORTEZOMIB 3.5 MG EUROLAB should use highly effective contraception, while being treated with BORTEZOMIB 3.5 MG EUROLAB and for an additional 5 months after taking the last dose.

Female patients and female sexual partners of male patients receiving BORTEZOMIB 3.5 MG EUROLAB should use highly effective contraception, while being treated with BORTEZOMIB 3.5 MG EUROLAB and an additional 8 months after taking the last dose.

If, despite these measures, pregnancy occurs, tell your doctor immediately.

Pregnancy

You should not use BORTEZOMIB 3.5 MG EUROLAB if you are pregnant, unless clearly necessary. If you become pregnant while receiving treatment, tell your doctor immediately.

Breast-feeding

You should not breast-feed while using BORTEZOMIB 3.5 MG EUROLAB. Discuss with your doctor when it is safe to restart breast-feeding after finishing your treatment.

Fertility

Fertility studies were not conducted with bortezomib.

Driving and using machines

BORTEZOMIB 3.5 MG EUROLAB might cause 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 BORTEZOMIB 3.5 MG EUROLAB may interfere with your daily activities. You should ensure that you do not engage in the above activities until you are aware of the measure to which BORTEZOMIB 3.5 MG EUROLAB affects you.

3 How to take BORTEZOMIB 3.5 MG EUROLAB

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

You will not be expected to give yourself BORTEZOMIB 3.5 MG EUROLAB. It will be given to you a person who is qualified to do so.

You will be given BORTEZOMIB 3.5 MG EUROLAB intravenously (into the vein) or subcutaneously (under the skin).

Your doctor will work out your dose of BORTEZOMIB 3.5 MG EUROLAB according to your height and weight (body surface area). Your doctor will also tell you how many treatment cycles you will have. You will have dosing days and rest days (where no treatment is given). 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).

Your doctor will tell you how long your treatment with BORTEZOMIB 3.5 MG EUROLAB will last. Do not stop treatment early. If you have the impression that the effect of BORTEZOMIB 3.5 MG EUROLAB is too strong or too weak, tell your doctor or pharmacist.

If you are given more BORTEZOMIB 3.5 MG EUROLAB than you should

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Since a healthcare professional will administer BORTEZOMIB 3.5 MG EUROLAB, he/she will control the dosage. However, in the event of overdosage your doctor will manage the overdosage.

If you forget to take BORTEZOMIB 3.5 MG EUROLAB

Since a healthcare provider will administer BORTEZOMIB 3.5 MG EUROLAB, it is unlikely that the dose will be missed.

4 Possible side effects

BORTEZOMIB 3.5 MG EUROLAB can have side effects.

Not all side effects reported for BORTEZOMIB 3.5 MG EUROLAB are included in this leaflet.

Should your general health worsen or if you experience any untoward effects while taking BORTEZOMIB 3.5 MG EUROLAB, please consult your health care provider for advice.

If any of the following happens, stop taking BORTEZOMIB 3.5 MG EUROLAB and tell your doctor immediately or go to the casualty department at your nearest hospital:

- If you develop sepsis. Symptoms include fever, difficulty breathing, low blood pressure, fast heart rate and mental confusion.
- Headache, fever, neck stiffness, seizures, confusion that can be signs of a brain infection or inflammation (meningitis).
- Fever, bruises or bleeding, swollen legs, decreased urine, confusion, sleepiness or seizures that can be signs of Thrombotic microangiopathy that can be life-threatening.
- Allergic reaction (hypersensitivity), symptoms can include swelling of the hands, feet, ankles, face, lips and mouth or throat which can cause difficulty in swallowing or breathing.

- Feeling lightheaded, difficulty breathing, wheezing, fast heartbeat, confusion, clammy skin. All can be signs of anaphylactic shock.
- Symptoms of nausea, vomiting, diarrhoea, muscle cramps, weakness and tiredness can be a sign of a life-threatening condition called Tumour lysis syndrome.
- Hypovolemia (liquid portion of the blood is too low). Symptoms include weakness, fatigue, fainting and dizziness.
- Numbness or weakness in part of the face, difficulty speaking or difficulty walking, loss of consciousness, double vision, nausea, vomiting, severe headache, trouble speaking, drooping eyelid, neck pain or stiffness, sudden lightheadedness with or without weakness.
- Heart failure, heart attack, chest pain or discomfort, heart palpitations, rapid, reduced or irregular heartbeat, wheezing, shortness of breath, fainting, dizziness, low blood pressure, sweating, pale skin, lightheadedness or fainting, confusion, swollen legs and feet, tiredness and weakness. All can be signs of heart complications.
- Leg pain or swelling, red or discoloured skin on the leg.
- Confusion, unconsciousness, cold, pale and clammy skin, thirst, muscle cramps, decrease in blood pressure (signs of cardiogenic shock).
- Lung embolism or fluid in lungs. Symptoms include shortness of breath, rapid breathing, low oxygen in the body, chest pain, cough, collapsed lung.
- Gastrointestinal perforation – symptoms include chills, fever, nausea and vomiting.
- Liver toxicity or bleeding – symptoms include a rash, stomach pain or swelling, nausea and vomiting, tiredness, dark-coloured urine, yellow skin and eyes, loss of appetite, general sense of feeling unwell, confusion.
- Life threatening skin condition, characterised by a blistering and peeling of the skin (Toxic skin eruption or Toxic epidermal necrolysis).
- Steven-Johnson syndrome - flu-like symptoms appear first, then a painful rash appears that spreads and blisters follow.

- Rhabdomyolysis – a life-threatening condition caused by muscle breakdown and muscle death. Symptoms include dark, reddish urine, a decreased amount of urine, weakness and muscle aches.
- Sudden kidney failure.

These are all very serious side effects listed above. If you have them, you may have had a serious reaction to BORTEZOMIB 3.5 MG EUROLAB. You may need urgent medical attention or hospitalisation.

Treatment with BORTEZOMIB 3.5 MG EUROLAB can very 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 BORTEZOMIB 3.5 MG EUROLAB, to check your blood cell counts regularly. You may experience a reduction in the number of:

- Platelets, which make you be more prone to bruising, or to bleeding without obvious injury (e.g., bleeding from your bowels, stomach, mouth and gums 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 immediately or go to the casualty department at your nearest hospital if you notice any of the following:

- Coughing, breathing difficulties or tightness in the chest, shortness of breath, chest pain or discomfort, dizziness, fever or chills, coughing up blood, abnormally rapid breathing or hyperventilation, feeling lightheaded, confusion and dry mouth. These are all symptoms of conditions affecting the lungs
- Abnormal bumps, unexplained fever, night sweats or unintentional weight loss

- Bone pain, enlarged liver or spleen
- Cancerous (malignant) or non-cancerous (benign) growth/cyst
- A scaly, red rash in areas of the body that usually are not exposed to the sun, sleeplessness
- Sudden flank or abdominal pain, blood in urine, low blood pressure and shock
- Cool, numb limbs and muscle pain are symptoms due to a blood clot that blocks blood flow
- Chronic kidney failure. Symptoms are gradual that includes feeling tired, high blood pressure, loss of appetite, or water-electrolyte imbalance

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:

- Shingles (localised including around the eyes or spread across the body)
- Infections, including pneumonia, respiratory infections, bronchitis, fungal infections, coughing with phlegm, flu-like illness
- Painful blisters in or around the mouth
- Skin rash, peeling, small bumps that may be itching or vaginal infection resulting in abnormal discharge, all can be a result of a fungal infection
- Decreased appetite
- Dehydration
- Diabetes mellitus. Symptoms include increased thirst, frequent urination, extreme hunger, unexplained weight loss, tiredness, irritability, blurred vision
- Mood, and anxiety disorders and disturbances
- Sleep disorders and disturbances

- Sensitivity, numbness, tingling or burning sensation of the skin, or pain in the hands or feet, due to nerve damage
- Abnormal sense of touch
- Stabbing, burning, and often severe pain due to an irritated or damaged nerve
- Loss of consciousness
- Dizziness
- Altered or impaired sense of taste
- Headache
- Eye swelling, abnormal or blurred vision
- Infection of the outermost layer of the eye and the inner surface of the eyelids (conjunctivitis)
- Vertigo (spinning sensation)
- Low blood pressure, sudden fall of blood pressure on standing which may lead to fainting
- High blood pressure
- Minor bleeding of the nose
- Nausea and vomiting, diarrhoea, constipation, indigestion
- Painful swelling and sores inside the mouth, bloating, throat pain, abdominal pain (including gastrointestinal and splenic pain), oral disorder, flatulence
- Gastrointestinal bleeding
- Stomach pain, dark urine, feeling tired, yellowing of your skin or eyes, light-coloured stools, loss of appetite, nausea and vomiting. All can be signs of abnormal liver enzymes
- Rash, itching, redness of the skin or dry skin
- Musculoskeletal pain or spasms
- Limb pain, muscle weakness
- Fever, feeling tired, weakness or lack of energy
- Water retention, chills, pain, general discomfort
- Weight loss

Less frequent side effects:

- Fever, chills, muscle aches, cough, congestion, runny nose, headaches and tiredness
- Urinary tract infection, the flu, skin, ear and tooth infections, cellulitis
- Tiredness, fever, inflamed throat, swollen lymph nodes in the neck, tenderness around spleen and liver area and a rash can be all signs of Epstein-Barr virus
- Painful, itchy sores on the genital area
- Tonsillitis – symptoms include a sore throat, difficulty swallowing and tender lymph nodes
- Ear infection that causes redness, swelling and tenderness around the ear, with possible fever, ear pain and discharge
- Chronic tiredness, sleep abnormalities, joint and muscle pain
- Bloody stools, or bleeding from mucosal membranes, e.g., mouth, vagina
- Small, red, bumps on the face, neck, and upper back
- Angioedema (fluid retention) – painless swelling underneath the skin, including arms and legs
- Amyloidosis (a rare disease that occurs when an abnormal protein, called amyloid, builds up in your organs. Symptoms depend on which organs are affected. They may include swelling, fatigue and weakness, shortness of breath, and numbness, tingling or pain in the hands or feet)
- Rash, arthritis, and fever, that can be signs of an immune complex reaction
- Fatty hump between the shoulders, a rounded face and pink or purple stretch marks
- Overactive thyroid. Symptoms include unexpected weight loss, rapid or irregular heartbeat, sweating and irritability
- Nausea and vomiting, headache, confusion, weakness and fatigue due to a condition in which high levels of a hormone causes the body to retain water

- Underactive thyroid. Symptoms include tiredness, cold sensitivity, constipation, dry skin and unexplained weight gain
- Failure to thrive
- Gout - symptoms include severe pain, redness and swelling in joints, often the big toe
- Increased appetite
- Alcohol intolerance
- Mental or psychotic disorder, including suicidal thoughts
- Hallucination, mental confusion and emotional disruption
- Restlessness
- Adjustment disorder
- Low libido
- Paralysis, seizures, falling, poor coordination, change in speech, movement disorders, abnormal or change in, or reduced sensation (feeling, hearing, tasting, smelling), difficulty swallowing, using arms, hands, legs or feet, abnormal reflexes
- Attention disturbance, memory loss, trembling, twitching, seizures, involuntary shaking or muscle movement
- Visual loss, headaches, limb weakness or numbness
- Occasional sharp, burning, shooting or burning pain, sensitivity to touch and temperature, itching, numbness and headaches can all be signs of post herpetic neuralgia after a shingles rash has healed
- Uncontrollable urge to move your legs
- Migraines
- Pain radiating from lower back through your hips and buttocks and down each leg
- Smell disorder
- Dizziness, fainting upon standing, sensation of fainting, inability to alter heart rate, sweating abnormalities

- Memory or language problems, decreased mental function, mood changes that can be signs of weakening of muscles
- Cerebrovascular disorders
- Pain, numbness, weakness or tingling of an extremity that can be due to spinal cord compression
- Drooling
- A red, painful lump near the edge of the eyelid that may look like a boil or pimple
- Bleeding eye, eye/eyelid infection or inflammation, dry eye, eye irritation or painful eye, eye discharge or excessive watering of eye
- Eye conditions/disorders that affects vision (lesion on cornea, retinitis, damage to optic nerve of the eye)
- Bulging eye, inflammation of the lacrimal eye gland
- Different degrees of visual impairment (double vision, blind spot or partial vision loss, eye sensitivity to light, eye floaters or flashes, blindness)
- Ear disorders, including hearing impairment (up to including deafness), ringing in ears, ear discomfort, bleeding in ears
- Sudden, severe vertigo
- Low blood pressure, shortness of breath and lightheadedness that can be signs of cardiac tamponade
- Flushing, increased blood flow causing redness, warmth or burning pain (including in the hands, feet and eyes)
- Inadequate blood circulation, particularly the legs and feet
- Vein discolouration or insufficiency
- Chest pain that worsens during breathing, hiccups, runny nose
- Disorder of the voice, wheezing
- Discomfort or temporary inability to breathe, especially when lying down or during sleeping

- Widening and rounding of the tips of the fingers or toes
- Throat tightness, dry throat, increased upper airway secretion, throat irritation
- Inflammation of the pancreas or intestines, vomiting blood
- Lip swelling or pain, painful sores in mouth, chapped lips
- Gastrointestinal obstruction, abdominal discomfort, stomach pain
- Bleeding or infected gums, coated tongue, swollen tongue, overgrown gums
- Acid reflux, difficulty or painful swallowing, burping, a feeling of early fullness
- Irritable bowel syndrome/ spastic colon
- Dry or bad taste in mouth, mouth lesions, painful jaw and/or compromised movement, making it difficult to chew
- Pain, tenderness, rigid abdominal muscles, fever, nausea and vomiting. All can be signs of peritonitis (inflammation of the abdominal wall)
- Abdominal swelling, chest pain when eating
- Unable to control bowel movements, weak anal sphincter
- Change of bowel habit or abnormal faeces, including hardened, accumulated faeces at the rectum or colon, passage of mucus or other liquid from the anus
- A small tear in the lining of the anus, painful spasms of the anal sphincter or muscles of the rectum
- Yellow skin or eyes (jaundice), nausea, vomiting, stomach pain and/or swelling, feeling tired, fever, dark urine and light-coloured bowel movements. These symptoms can all be signs of liver conditions
- Bleeding in the oesophagus, gallstones
- Painful, red, scaly or itchy skin mostly on arms, face, neck and scalp
- Red, itchy or scaly rash, pimple-like eruptions or inflammation of the skin
- Hair, or nail disorders
- Tiny round, brown-purple spots due to bleeding under the skin or bruising of the skin

- Photosensitivity or rare, non-cancerous papular or plaque-like eruptions on the skin
(commonly involve sun-exposed areas), hand-foot syndrome (redness, swelling and blistering on the palms of the hands and soles of the feet)
- Excessive sweating, night or cold sweats
- Bed sores, acne, blisters, small raised tender bumps or open round sores
- Netlike pattern of reddish-blue skin discoloration and pigmentation disorder
- Deep thickening of the skin
- Muscle twitching, joint swelling, arthritis, joint stiffness
- Muscle weakness, cramps, lack of energy and feeling tired
- Bone disorder
- Muscle and connective tissue infection and inflammation
- Blood in urine, urinary retention or abnormalities when urinating
- Frequent or non-frequent urination, painful urination, shortness of breath, feeling tired, nausea and vomiting, swelling of face, feet or ankles, muscle cramps, confusion, weakness, excessive drinking of fluids
- Abnormal vaginal bleeding, genital pain or sores in vaginal area
- Erectile dysfunction, testicle disorder, swelling or inflammation of the prostate gland, testicle pain and tenderness
- Breast disorder in women
- Pelvic pain
- General physical health deterioration
- Injection site reaction, bleeding, inflammation or pain
- Chest pain or discomfort, feeling cold
- Abnormal walking, change in thirst, irritability
- Catheter related complication, catheter site pain
- Feeling of change in body temperature, sensation of foreign body
- Hernia, impaired healing, inflammation, tenderness

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- Ulcers or sores on the lining of your stomach or small intestine
- Increase in weight or a sensation of heaviness
- Fall, bruises, fractures, face or joint injury, burns, laceration or skin wound, procedural pain

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. You can also report side effects to SAHPRA via the Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on SAHPRA website or to Eurolab (Pty) Ltd. by email: drug-safety@eurolab.co.za. By reporting side effects, you can help provide more information on the safety of BORTEZOMIB 3.5 MG EUROLAB.

5 How to store BORTEZOMIB 3.5 MG EUROLAB

- Store all medicines out of reach of children.
- Store at or below 30 °C. Keep in the outer carton in order to protect from light, until required for use.
- Do not use after the expiry date stated on the label / carton.
- Do not use BORTEZOMIB 3.5 MG EUROLAB if you notice any visible signs of deterioration.
- Return all unused medicine to your pharmacist.
- Do not dispose of unused medicine in drains or sewerage systems (e.g. toilets).

Shelf-life

24 months

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6 Contents of the pack and other information

What BORTEZOMIB 3.5 MG EUROLAB contains

The active substance is bortezomib.

The other ingredients are mannitol and nitrogen.

What BORTEZOMIB 3.5 MG EUROLAB looks like and contents of the pack

BORTEZOMIB 3.5 MG EUROLAB is packed in 10 ml Type I clear glass vials, closed with grey bromobutyl rubber stoppers and grey aluminium caps, fitted with red plastic flip-off disc.

Holder of Certificate of Registration

Eurolab (Pty) Ltd.

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