

PATIENT INFORMATION LEAFLET

SCHEDULING STATUS

S4

ZOBONE SOLUTION FOR INFUSION
(concentrate for solution for infusion)
Zoledronic acid
Contains 24 mg sodium per vial

Read all of this leaflet carefully before you are given ZOBONE SOLUTION FOR INFUSION

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

What is in this leaflet

1. What ZOBONE SOLUTION FOR INFUSION is and what it is used for
2. What you need to know before you use ZOBONE SOLUTION FOR INFUSION
3. How to use ZOBONE SOLUTION FOR INFUSION
4. Possible side effects
5. How to store ZOBONE SOLUTION FOR INFUSION
6. Contents of the pack and other information

1. What ZOBONE SOLUTION FOR INFUSION is and what it is used for

ZOBONE SOLUTION FOR INFUSION contains the active substance zoledronic acid, which belongs to a group of medicines called bisphosphonates. ZOBONE SOLUTION FOR INFUSION works by attaching itself to the bone and slowing down the rate of bone change. It is used for the following:

- Treatment of tumour-induced hypercalcaemia (TIH).
- ZOBONE SOLUTION FOR INFUSION slows progression of skeletal conditions in adult patients when used in conjunction with appropriate antineoplastic therapy in patients with advanced carcinoma of the

breast, prostate, lung and myeloma.

2. What you need to know before you use ZOBONE SOLUTION FOR INFUSION

ZOBONE SOLUTION FOR INFUSION should not be administered to you:

- if you are hypersensitive (allergic) to zoledronic acid or any of the other ingredients of ZOBONE SOLUTION FOR INFUSION (listed in section 6).
- if you suffer from severely impaired kidney function.
- if you are pregnant or breastfeeding (see Pregnancy, breastfeeding and fertility).

Warnings and precautions

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

Special care should be taken with ZOBONE SOLUTION FOR INFUSION:

- if you have or have had a kidney or liver problem
- if you have or have had pain, swelling or numbness of the jaw, a feeling of heaviness in the jaw or loosening of a tooth. Your doctor may recommend a dental examination before you start treatment with ZOBONE SOLUTION FOR INFUSION
- if you are having dental treatment or are due to undergo dental surgery, tell your dentist that you are being treated with ZOBONE SOLUTION FOR INFUSION and inform your doctor about your dental treatment
- If you had or have joint stiffness, aches and pains and difficulty in movement (especially of the hip or thigh) or bone disorders
- If you experience pain in the muscles or bones while being treated with ZOBONE SOLUTION FOR INFUSION.

Your doctor will perform regular blood tests to evaluate blood levels of certain minerals, such as calcium, phosphate, and magnesium, as well as serum creatinine (a marker of kidney function) after you have been started on ZOBONE SOLUTION FOR INFUSION therapy. Based on these results, your doctor may decide to prescribe mineral supplements for you, if indicated.

While being treated with ZOBONE SOLUTION FOR INFUSION, you should maintain good oral hygiene (including regular teeth brushing) and receive routine dental check-ups. Contact your doctor and dentist immediately if you experience any problems with your mouth or teeth such as loose teeth, pain or swelling, or

non-healing of sores or discharge, as these could be signs of a condition called osteonecrosis of the jaw.

If you are undergoing chemotherapy and/or radiotherapy, taking steroids, undergoing dental surgery, do not receive routine dental care, have gum disease, are a smoker or were previously treated with a bisphosphonate (used to treat or prevent bone disorders) may have a higher risk of developing osteonecrosis of the jaw.

Reduced levels of calcium in the blood (hypocalcaemia), sometimes leading to muscle cramps, dry skin, burning sensation, have been reported in patients treated with ZOBONE SOLUTION FOR INFUSION. Irregular heart beat (cardiac arrhythmia), seizures, spasm and twitching (tetany) have been reported as secondary to severe hypocalcaemia. In some instances the hypocalcaemia may be life-threatening. If any of these apply to you, tell your doctor straight away. If you have pre-existing hypocalcaemia, it must be corrected before initiating the first dose of ZOBONE SOLUTION FOR INFUSION. You will be given adequate calcium and vitamin D supplements

Children and adolescents

ZOBONE SOLUTION FOR INFUSION is not recommended for use in adolescents and children below the age of 18 years.

Other medicines and ZOBONE SOLUTION FOR INFUSION

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

- Aminoglycosides (medicines used to treat severe infections), calcitonin (a type of medicine used to treat post-menopausal osteoporosis and hypercalcaemia), loop diuretics (a type of medicine to treat high blood pressure or oedema) or other calcium-lowering medicines, since the combination of these with bisphosphonates may cause the calcium level in the blood to become too low.
- Thalidomide (a medicine used to treat a certain type of blood cancer involving the bone) or any other medicines which may harm your kidneys.
- Anti-angiogenic medicines (used to treat cancer), since the combination of these with ZOBONE SOLUTION FOR INFUSION has been associated with an increased risk of osteonecrosis of the jaw

(ONJ).

- Medicines used to treat cancer, blood pressure, infections and pain

Pregnancy, breastfeeding and fertility

If you are pregnant or breastfeeding, think you may be pregnant or are planning to have a baby, please consult your doctor, pharmacist or other healthcare provider for advice before taking this medicine.

You should not be given ZOBONE SOLUTION FOR INFUSION if you are pregnant.

You must not be given ZOBONE SOLUTION FOR INFUSION if you are breast-feeding.

Driving and using machines

There have been very rare cases of drowsiness and sleepiness with the use of ZOBONE SOLUTION FOR INFUSION. You should therefore be careful when driving, using machinery or performing other tasks that need full attention. The medicine may affect your vision.

ZOBONE SOLUTION FOR INFUSION contains sodium

This medicine contains 24 mg sodium (main component of cooking/table salt) in each vial This is equivalent to 1, 2 % of the recommended maximum daily dietary intake of sodium for an adult.

Tell your doctor if you are on a controlled sodium diet.

3. How to use ZOBONE SOLUTION FOR INFUSION

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

ZOBONE SOLUTION FOR INFUSION must only be given by healthcare professionals trained in administering bisphosphonates intravenously, i.e. through a vein. Your doctor will recommend that you drink enough water before each treatment to help prevent dehydration.

The usual single dose given is 4 mg.

If you have a kidney problem, your doctor will give you a lower dose depending on the severity of your kidney problem.

If you are being treated for the prevention of bone complications due to bone metastases (cancer spreading to your bones), you will be given one infusion of ZOBONE SOLUTION FOR INFUSION every three to four weeks.

If you are being treated to reduce the amount of calcium in your blood, you will normally only be given one infusion of ZOBONE SOLUTION FOR INFUSION.

ZOBONE SOLUTION FOR INFUSION is given as a drip (infusion) into a vein which should take at least 15 minutes and should be administered as a single intravenous solution in a separate infusion line.

Patients whose blood calcium levels are not too high will also be prescribed calcium and vitamin D supplements to be taken each day.

If you have the impression that ZOBONE SOLUTION FOR INFUSION is too strong or too weak for you, please discuss this with your treating doctor.

If you are given more ZOBONE SOLUTION FOR INFUSION than you should

Since a healthcare provider will administer ZOBONE SOLUTION FOR INFUSION, he / she will control the dosage. However, in the event of overdosage your doctor will manage the overdosage.

If you have received doses higher than those recommended, you must be carefully monitored by your doctor.

This is because you may develop serum electrolyte abnormalities (e.g. abnormal levels of calcium, phosphorus and magnesium) and/or changes in kidney function, including severe kidney impairment. If your level of calcium falls too low, you may have to be given supplemental calcium by infusion.

If you forget to use ZOBONE SOLUTION FOR INFUSION

Since a healthcare provider will administer ZOBONE SOLUTION FOR INFUSION, it is unlikely that the dose will be missed.

4. Possible side effects

ZOBONE SOLUTION FOR INFUSION can have side effects.

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

If any of the following happens, stop using ZOBONE SOLUTION FOR INFUSION powder for solution for infusion and tell your doctor immediately or go to the casualty department at your nearest hospital:

Frequent side effects:

- Swelling of the face, lips, mouth, tongue or throat which may cause difficulty in swallowing or breathing (angioedema/ Hypersensitivity reaction).

Less frequent side effects:

- Sudden signs of allergy such as rash, itching or hives on the skin, swelling of the face, lips, tongue or other parts of the body, shortness of breath, wheezing or trouble breathing, as these may be signs of a serious allergic (anaphylactic) reaction
- Low blood pressure leading to fainting or circulatory collapse
- Pain in the mouth, teeth and/or jaw, swelling or non-healing sores inside the mouth or jaw, discharge, numbness or a feeling of heaviness in the jaw, or loosening of a tooth. These could be signs of bone damage in the jaw (osteonecrosis). Also seen occurring with other bones than the jaw, especially the hip or thigh

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

Tell your doctor immediately or go to the casualty department at your nearest hospital if you notice any of the following:

Frequent side effects:

- Inflammation of the tissue around the air sacks of the lungs
- (Interstitial lung disease)
- Blood in the urine (haematuria), painful or difficult release of urine
- Chest pain

Less Frequent side effects:

- Slow heart beat (Bradycardia)
- Fast heart beat (atrial fibrillation)
- As a consequence of low calcium values: irregular heart beat (cardiac arrhythmia; secondary to hypocalcaemia)

Frequency not known side effects:

- Tightness or pain in the chest (bronchoconstriction)
- A kidney function disorder called Fanconi syndrome (will normally be determined by your doctor with certain urine tests)
- Kidney problems, little or no urine, drowsiness, nausea, vomiting, breathlessness (acute renal failure)
- If protein is found in your urine (proteinuria)
- Severe kidney impairment (will normally be determined by your doctor with certain specific blood tests)

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:

- Low blood platelet count, symptoms include bleeding or bruising more easily than normal (thrombocytopenia)
- Decrease in the number of white blood cells (anaemia)
- A rare type of anaemia in which the red blood cells, white blood cells and platelets are all reduced in number (pancytopenia)
- Sweating, trembling, feeling nervous or anxious, fast heart beat (anxiety)
- Sleep disturbance
- Headache
- Dizziness
- Tingling or numbness of the hands or feet (paraesthesia)
- Decreased feeling or sensitivity, especially in the skin (Hypoaesthesia)
- Shortness of breath, difficulty in breathing, chest tightness (dyspnoea)

- Cough
- Nausea, vomiting, loss of appetite (anorexia), loss stool (diarrhea), abdominal pain
- Constipation, dry mouth
- Increased sweating
- Aching muscles, muscle tenderness or weakness, not caused by exercise (myalgia)
- Joint pain, painful, swollen joints (arthralgia)
- Muscle cramps
- Pain
- A flu-like syndrome consisting of fever, fatigue, weakness, drowsiness, chills and bone, joint and/or muscle ache
- Low levels of phosphate in the blood (hypophosphataemia)
- Low calcium levels in the blood serum (hypocalcaemia)
- Low magnesium levels in the blood serum (hypomagnesaemia)
- Low potassium levels in the blood serum (hypokalaemia)

Less frequent side effects:

- Taste disturbance
- Sleepiness and drowsiness (somnolence)
- Blurred vision, tearing of the eye, eye sensitivity to light (scleritis and orbital inflammation, uveitis)
- Change in blood pressure (hypertension, hypotension)
- disease mainly affecting the joints with pain and swelling, painful joint disease (arthritis)

Frequency not known side effects:

- Lack of white blood cells (leucopenia)
- Confusion
- Increased feeling or sensitivity, especially in the skin (hyperaesthesia)
- shaking or tremors
- Fits (convulsions)
- Spasm and twitching (tetany) (secondary to hypocalcaemia)
- Conjunctivitis

- Blurred vision, tearing of the eye, eye sensitivity to light (episcleritis)
- An uncomfortable feeling in the stomach or belching after eating, indigestion (dyspepsia)
- Sore mouth, mouth ulcers and cold sores (stomatitis)
- Swelling of hands, ankles or feet
- Injection site reactions (including pain, irritation, swelling)
- Weight increase
- Increased blood creatinine and blood urea
- High potassium levels in the blood serum (hyperkalaemia)
- High concentration of sodium in the blood (hypernatraemia)

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 nurses. This includes any possible side effects not listed in this leaflet. You can also report side effects to SAHPRA via the “**6.04 Adverse Drug 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 ZOBONE SOLUTION FOR INFUSION.

5. How to store ZOBONE SOLUTION FOR INFUSION

- Store below 25 °C.
- The ZOBONE SOLUTION FOR INFUSION solution is stable for 24 hours at 2 °C – 8 °C after further dilution.
- KEEP ALL MEDICINES OUT OF REACH OF CHILDREN.
- Do not use the concentrate for infusion after the expiry date printed on the container or label.
- Return all unused medicine to your pharmacist
- Do not dispose of unused medicine in drains and sewerage systems (e.g. toilets)

6. Contents of the pack and other information

What ZOBONE SOLUTION FOR INFUSION contains

The active substance is zoledronic acid.

The other ingredients are: Mannitol, Sodium citrate, water for injection

What ZOBONE SOLUTION FOR INFUSION looks like and contents of the pack

Clear colourless solution in 5 mL colourless tubular glass vial with grey rubber stopper sealed with baby blue flip top aluminum seal.

Vial: 5 ml clear Type-I Neutral glass vial.

Stopper: Grey bromobutyl flange rubber stopper.

Seal: White aluminium seal and baby blue flip top aluminium seal.

Packed in unit packs containing 1x 5 mL single vial.

Holder of Certificate of Registration

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This leaflet was revised in

10 August 2022

Registration number

47/34/1168