Package leaflet: information for the user

Zoledronic acid Sandoz 4 mg/5 ml Concentrate for Solution for Infusion

Zoledronic acid

Read all of this leaflet carefully before you are given this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, nurse or pharmacist.
- If you get any side effects, talk to your doctor, nurse or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

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1 What Zoledronic acid Sandoz is and what it is used for

The active substance in Zoledronic acid Sandoz is zoledronic acid, which belongs to a group of substances called bisphosphonates. Zoledronic acid works by attaching itself to the bone and slowing down the rate of bone change. It is used:
- **To prevent bone complications,** e.g. fractures, in adult patients with **bone metastases** (spread of cancer from primary site to the bone).
- **To reduce the amount of calcium** in the blood in adult patients where it is too high due to the presence of a tumour. Tumours can accelerate normal bone change in such a way that the release of calcium from bone is increased. This condition is known as tumour-induced hypercalcaemia (TIH).

2 What you need to know before you are given Zoledronic acid Sandoz

Follow carefully all instructions given to you by your doctor.

Your doctor will carry out blood tests before you start treatment with Zoledronic acid Sandoz and will check your response to treatment at regular intervals.

You should not be given Zoledronic acid Sandoz
- if you are breast-feeding
- if you are allergic to zoledronic acid, another bisphosphonate (the group of substances to which Zoledronic acid Sandoz belongs), or any of the other ingredients of this medicine (listed in section 6).

Warnings and precautions
Talk to your doctor before you are given Zoledronic acid Sandoz
- if you have or have had a **kidney 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 Zoledronic acid Sandoz.
- if you are having **dental treatment** or are due to undergo dental surgery, tell your dentist that you are being treated with Zoledronic acid Sandoz and inform your doctor about your dental treatment.

While being treated with Zoledronic acid Sandoz, 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.

Patients who are undergoing chemotherapy and/ or radiotherapy, who are taking steroids, who are undergoing dental surgery, who do not receive routine dental care, who have gum disease, who are smokers, or who 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 Zoledronic acid Sandoz. Irregular heartbeat (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 Zoledronic acid Sandoz. You will be given adequate calcium and vitamin D supplements.

Patients aged 65 years and over
Zoledronic acid Sandoz can be given to people aged 65 years and over. There is no evidence to suggest that any extra precautions are needed.

Children and adolescents
Zoledronic acid Sandoz is not recommended for use in children and adolescents below the age of 18 years.

Other medicines and Zoledronic acid Sandoz
Tell your doctor if you are taking, have recently taken or might take any other medicines. It is especially important that you tell your doctor if you are also taking:
- 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.
- Other medicines that also contain zoledronic acid and are used to treat osteoporosis and other non-cancer diseases of the bone, or any other bisphosphonate, since the combined effects of these medicines taken together with Zoledronic acid Sandoz are unknown.
- Anti-angiogenic medicines (used to treat cancer), since the combination of these medicines with zoledronic acid has been associated with an increased risk of osteonecrosis of the jaw (ONJ).

Pregnancy and breast-feeding
You should not be given Zoledronic acid Sandoz if you are pregnant. Tell your doctor if you are or think that you may be pregnant.

You must not be given Zoledronic acid Sandoz if you are breast-feeding.

Ask your doctor for advice before taking any medicine while you are pregnant or breast-feeding.

Driving and using machines
There have been very rare cases of drowsiness and sleepiness with the use of zoledronic acid. You should therefore be careful when driving, using machinery or performing other tasks that need full attention.

Zoledronic acid Sandoz contains sodium.
This medicinal product contains less than 1 mmol sodium (23 mg) per dose, i.e. essentially 'sodium- free'.

3 How Zoledronic Acid Sandoz is used

- Zoledronic acid Sandoz 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.
- Carefully follow all the other instructions given to you by your doctor, nurse or pharmacist.

How much Zoledronic acid Sandoz is given
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.

How often Zoledronic acid Sandoz is given
- If you are being treated for the prevention of bone complications due to bone metastases, you will be given one infusion of Zoledronic acid Sandoz 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 Zoledronic acid Sandoz.

How Zoledronic acid Sandoz is given
- Zoledronic acid Sandoz 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 are given more Zoledronic acid Sandoz than you should be
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.

4 Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them. The most common ones are usually mild and will probably disappear after a short time.

Tell your doctor about any of the following serious side effects straight away:

Common (may affect up to 1 in 10 people):
- Severe kidney impairment (will normally be determined by your doctor with certain specific blood tests).
- Low level of calcium in the blood.

Uncommon (may affect up to 1 in 100 people):
- 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). Tell your doctor and dentist immediately if you experience such symptoms while being treated with Zoledronic acid Sandoz or after stopping treatment.
- Irregular heart rhythm (atrial fibrillation) has been seen in patients receiving zoledronic acid for postmenopausal osteoporosis. It is currently unclear whether zoledronic acid causes this irregular heart rhythm but you should report it to your doctor if you experience such symptoms after you have received zoledronic acid.

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- Severe allergic reaction: shortness of breath, swelling mainly of the face and throat.

Rare (may affect up to 1 in 1,000 people):
- As a consequence of low calcium values: irregular heartbeat (cardiac arrhythmia; secondary to hypocalcaemia).
- A kidney function disorder called Fanconi syndrome (will normally be determined by your doctor with certain urine tests).

Very rare (may affect up to 1 in 10,000 people):
- As a consequence of low calcium values: seizures, numbness and tetany (secondary to hypocalcaemia).
- Talk to your doctor if you have ear pain, discharge from the ear, and/or an ear infection. These could be signs of bone damage in the ear.
- Osteonecrosis has also very rarely been seen occurring with other bones than the jaw, especially the hip or thigh. Tell your doctor immediately if you experience symptoms such as new onset or worsening of aches, pain or stiffness while being treated with Zoledronic acid Sandoz or after stopping treatment.

Tell your doctor about any of the following side effects as soon as possible:

Very common (may affect more than 1 in 10 people):
- Low level of phosphate in the blood.

Common (may affect up to 1 in 10 people):
- Headache and a flu-like syndrome consisting of fever, fatigue, weakness, drowsiness, chills and bone, joint and/or muscle ache. In most cases no specific treatment is required and the symptoms disappear after a short time (couple of hours or days).
- Gastrointestinal reactions such as nausea and vomiting as well as loss of appetite.
- Conjunctivitis.
- Low level of red blood cells (anaemia).

Uncommon (may affect up to 1 in 100 people):
- Hypersensitivity reactions
- Low blood pressure.
- Chest pain.
- Skin reactions (redness and swelling) at the infusion site, rash, itching.
- High blood pressure, shortness of breath, dizziness, anxiety, sleep disturbances, taste disturbances, trembling, tingling or numbness of the hands or feet, diarrhoea, constipation, abdominal pain, dry mouth.
- Increased sweating.
- Low counts of white blood cells and blood platelets.
- Low level of magnesium and potassium in the blood. Your doctor will monitor this and take any necessary measures.
- Weight increase.
- Sleepiness.
- Blurred vision, tearing of the eye, eye sensitivity to light.
- Sudden coldness with fainting, limpness or collapse.
- Difficulty in breathing with wheezing or coughing.
- Urticaria.

Rare (may affect up to 1 in 1,000 people):
- Slow heartbeat.
- Confusion.
- Unusual fracture of the thigh bone particularly in patients on long-term treatment for osteoporosis may occur rarely. Contact your doctor if you experience pain, weakness or discomfort in your thigh, hip or groin as this may be an early indication of a possible fracture of the thigh bone.
- Interstitial lung disease (inflammation of the tissue around the air sacks of the lungs).
- Flu-like symptoms including arthritis and joint swelling.
- Painful redness and/or swelling of the eye.

Very rare (may affect up to 1 in 10,000 people):
- Fainting due to low blood pressure.
- Severe bone, joint and/or muscle pain, occasionally incapacitating.

Reporting of side effects
If you get any side effects talk to your doctor, nurse or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via HPRA Pharmacovigilance; website: www.hpra.ie. By reporting side effects you can help provide more information on the safety of this medicine.

5 How to store Zoledronic acid Sandoz

Keep this medicine out of the sight and reach of children.

Your doctor, nurse or pharmacist knows how to store this medicine properly.

Do not use this medicine after the expiry date which is stated on the carton and on the bottle. The expiry date refers to the last days of that month.

This medicinal product does not require any special storage conditions.

After first opening, the product should be used immediately. Discard any unused contents.
Do not use this medicine if you notice any visible signs of deterioration such as particles and discolouration.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6 Contents of the pack and other information

What Zoledronic acid Sandoz contains
The active substance is zoledronic acid. One vial of 5 ml concentrate for solution for infusion contains 4 mg zoledronic acid, corresponding to 4.264 mg zoledronic acid monohydrate. 1 ml concentrate for solution for infusion contains 0.8 mg zoledronic acid

The other ingredients are mannitol (E421), sodium citrate (E331), water for injections.

What Zoledronic acid Sandoz looks like and contents of the pack
Zoledronic acid Sandoz is supplied as a clear and colourless liquid concentrate in a vial. One vial contains 4 mg of zoledronic acid.

Each pack contains the vial with concentrate. Zoledronic acid Sandoz is supplied as packs containing 1, 4 or 10 vials. Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturers
Marketing Authorisation Holder
Rowex Ltd., Bantry, Co. Cork, Ireland.

Manufacturers
Lek Pharmaceuticals d.d., Verovškova 57, 1526 Ljubljana, Slovenia.
Ebewe Pharma GmbH Nfg. KG, Mondseestrasse 11, A-4866 Unterach, Austria.
Novartis Pharma GmbH, Roonstrasse 25 und Obere Turnstrasse 8; 90429 Nurnberg, Germany.
Lek S.A., Podlipie 16, 95-010 Stryków, Poland.

This medicinal product is authorised in the Member States of the EEA under the following names:

Austria	Zoledronsäure Sandoz 4 mg/5 ml – Konzentrat zur Herstellung einer Infusionslösung
Bulgaria	ЗОЛЕДРОНОВА КИСЕЛИНА САНДОЗ 4 MG/5 ML КОНЦЕНТРАТ ЗА ИНФУЗИОНЕН РАЗТВОР
Finland	Zoledronic Acid Sandoz 4 mg / 5 ml infuusiokonsentraatti, liuosta varten
Ireland	Zoledronic acid Sandoz 4 mg/5 ml Concentrate for Solution for Infusion
Italy	Acido Zoledronico Sandoz
Malta	Zoledronic acid Sandoz 4 mg/5ml concentrate for solution for infusion
Portugal	Ácido Zoledrónico Sandoz
Romania	ACID ZOLEDRONIC SANDOZ 4 mg/5 ml concentrat pentru soluție perfuzabilă
Sweden	Zoledronic acid Sandoz 4 mg/5 ml koncentrat till infusionsvätska, lösning
Slovenia	Zoledronska kislina Sandoz 4 mg/5 ml koncentrat za raztopino za infundiranje
Slovakia	Kyselina zoledrónová Sandoz 4 mg/5 ml infúzny koncentrát
United Kingdom	Zoledronic acid Sandoz 4 mg/5ml concentrate for solution for infusion

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INFORMATION FOR THE HEALTHCARE PROFESSIONAL

How to prepare and administer Zoledronic acid Sandoz
- To prepare an infusion solution containing 4 mg zoledronic acid, further dilute the Zoledronic acid Sandoz concentrate (5.0 ml) with 100 ml of calcium-free or other divalent cation-free infusion solution. If a lower dose of Zoledronic acid Sandoz is required, first withdraw the appropriate volume as indicated below and then dilute it further with 100 ml of infusion solution. To avoid potential incompatibilities, the infusion solution used for dilution must be either 0.9% w/v sodium chloride or 5% w/v glucose solution.

Do not mix Zoledronic acid Sandoz concentrate with calcium-containing or other divalent cation-containing solutions such as lactated Ringer's solution.

Instructions for preparing reduced doses of Zoledronic acid Sandoz:
Withdraw the appropriate volume of the liquid concentrate, as follows:
- 4.4 ml for 3.5 mg dose
- 4.1 ml for 3.3 mg dose
- 3.8 ml for 3.0 mg dose

- For single use only. Any unused solution should be discarded. Only clear solution free from particles and discolouration should be used. Aseptic techniques must be followed during the preparation of the infusion.
- Studies with several types of infusion lines made from polyvinylchloride, polyethylene and polypropylene showed no incompatibility with Zoledronic acid Sandoz.
- Since no data are available on the compatibility of Zoledronic acid Sandoz with other intravenously administered substances, Zoledronic acid Sandoz must not be mixed with other medications/substances and should always be given through a separate infusion line.
- Zoledronic acid Sandoz 4 mg concentrate for solution for infusion, further diluted in 100 ml, should be given as a single intravenous infusion in no less than 15 minutes in a separate infusion line. The hydration status of patients must be assessed prior to and following administration of Zoledronic acid Sandoz to ensure that they are adequately hydrated.

How to store Zoledronic acid Sandoz
- Keep Zoledronic acid Sandoz out of the sight and reach of children.
- Do not use Zoledronic acid Sandoz after the expiry date stated on the pack.
- The unopened vial does not require any specific storage conditions.
- The diluted Zoledronic acid Sandoz infusion solution should be used immediately in order to avoid microbial contamination.