

## **PACKAGE LEAFLET: INFORMATION FOR THE USER**

### **Zoledronic Acid 5mg/100 ml 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, pharmacist or nurse.
- If you get any side effects talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

#### **What is in this leaflet**

1. What Zoledronic Acid is and what it is used for
2. What you need to know before you are given Zoledronic Acid
3. How Zoledronic Acid is given
4. Possible side effects
5. How to store Zoledronic Acid
6. Contents of the pack and other information

### **1. WHAT ZOLEDRONIC ACID IS AND WHAT IT IS USED FOR**

Zoledronic Acid 5 mg/100 ml solution for infusion contains the active substance zoledronic acid. It belongs to a group of medicines called bisphosphonates and is used to treat post-menopausal women and adult men with osteoporosis or osteoporosis caused by treatment with steroids, and Paget's disease of the bone in adults.

#### **Osteoporosis**

Osteoporosis is a disease that involves the thinning and weakening of the bones and is common in women after the menopause, but can also occur in men. At the menopause, a woman's ovaries stop producing the female hormone oestrogen, which helps keep bones healthy. Following the menopause bone loss occurs, bones become weaker and break more easily. Osteoporosis could also occur in men and women because of the long term use of steroids, which can affect the strength of bones. Many patients with osteoporosis have no symptoms but they are still at risk of breaking bones because osteoporosis has made their bones weaker. Decreased circulating levels of sex hormones, mainly oestrogens converted from androgens, also play a role in the more gradual bone loss observed in men. In both women and men, Zoledronic Acid strengthens the bone and therefore makes it less likely to break. Zoledronic Acid is also used in patients who have recently broken their hip in a minor trauma such as a fall and therefore are at risk of subsequent bone breaks.

#### **Paget's disease of the bone**

It is normal that old bone is removed and is replaced with new bone material. This process is called remodelling. In Paget's disease, bone remodelling is too rapid and new bone is formed in a disordered fashion, which makes it weaker than normal. If the disease is not treated, bones may become deformed and painful, and may break. Zoledronic Acid works by returning the bone remodelling process to normal, securing formation of normal bone, thus restoring strength to the bone.

### **2. WHAT YOU NEED TO KNOW BEFORE YOU ARE GIVEN ZOLEDRONIC ACID**

Follow all instructions given to you by your doctor, pharmacist or nurse carefully before you are given Zoledronic Acid.

**You must not be given Zoledronic Acid:**

- if you are allergic to zoledronic acid, other bisphosphonates or any of the other ingredients of this medicine (listed in section 6).
- if you have hypocalcaemia (this means that the levels of calcium in your blood are too low).
- if you have severe kidney problems.
- if you are pregnant.
- if you are breast-feeding.

**Warnings and precautions**

Talk to your doctor before you are given Zoledronic Acid:

- if you are being treated with Zoledronic Acid 4mg/100ml solution for infusion or Zoledronic acid 4mg/5ml concentrate for solution for infusion, which contains the same active substance as Zoledronic Acid and are used in adult patients with certain types of cancer to prevent bone complications or to reduce the amount of calcium.
- if you have a kidney problem, or used to have one.
- if you are unable to take daily calcium supplements.
- if you have had some or all of the parathyroid glands in your neck surgically removed.
- if you have had sections of your intestine removed.

Before you receive treatment with Zoledronic Acid, tell your doctor if you have (or have had) pain, swelling or numbness in your gums, jaw or both, if your jaw feels heavy, or if you have lost a tooth. Before you receive dental treatment or undergo dental surgery, tell your dentist you are receiving treatment with Zoledronic Acid.

**Monitoring test**

Your doctor should do a blood test to check your kidney function (levels of creatinine) before each dose of Zoledronic Acid. It is important for you to drink at least 2 glasses of fluid (such as water), within a few hours before receiving Zoledronic Acid, as directed by your healthcare provider.

**Children and adolescents**

Zoledronic Acid is not recommended for anyone under 18 years of age. The use of Zoledronic Acid in children and adolescents has not been studied.

**Other medicines and Zoledronic Acid**

Tell your doctor, pharmacist or nurse if you are taking, have recently taken or might take any other medicines.

It is especially important for your doctor to know all the medicines you are taking, especially if you are taking any medicines known to be harmful to your kidneys (e.g. aminoglycosides) or diuretics (“water pills”) that may cause dehydration.

**Pregnancy and breast-feeding**

You must not be given Zoledronic Acid if you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby.

Ask your doctor, pharmacist or nurse for advice before taking this medicine.

#### **Driving and using machines**

Zoledronic Acid has no or negligible influence on the ability to drive and use machines. If you feel dizzy while taking Zoledronic Acid, do not drive or use machines until you feel better.

#### **Zoledronic Acid contains sodium.**

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

### **3. HOW ZOLEDRONIC ACID IS GIVEN**

Follow carefully all instructions given to you by your doctor or nurse. Check with your doctor or nurse if you are not sure.

#### **Osteoporosis**

The usual dose is 5 mg given as one infusion per year into a vein by your doctor or nurse. The infusion will take at least 15 minutes.

In case you recently broke your hip, it is recommended that Zoledronic Acid is administered two or more weeks after your hip repair surgery.

It is important to take calcium and vitamin D supplements (for example tablets) as directed by your doctor.

For osteoporosis, Zoledronic Acid works for one year. Your doctor will let you know when to return for your next dose.

#### **Paget's disease**

The usual dose is 5 mg, given to you as one initial infusion into a vein by your doctor or nurse. The infusion will take at least 15 minutes. Zoledronic Acid may work for longer than one year, and your doctor will let you know if you need to be treated again.

Your doctor may advise you to take calcium and vitamin D supplements (e.g. tablets) for at least the first ten days after being given Zoledronic Acid. It is important that you follow this advice carefully so that the level of calcium in your blood does not become too low in the period after the infusion. Your doctor will inform you regarding the symptoms associated with hypocalcaemia.

#### **Zoledronic Acid with food and drink**

Make sure you drink enough fluids (at least one or two glasses) before and after the treatment with Zoledronic Acid, as directed by your doctor. This will help to prevent dehydration. You may eat normally on the day you are treated with Zoledronic Acid. This is especially important in patients who take diuretics ("water pills") and in elderly patients.

#### **If you missed a dose of Zoledronic Acid**

Contact your doctor or hospital as soon as possible to re-schedule your appointment.

#### **Before stopping Zoledronic Acid therapy**

If you are considering stopping Zoledronic Acid treatment, please go to your next appointment and discuss this with your doctor. Your doctor will advise you and decide how long you should be treated with Zoledronic Acid.

If you have any further questions on the use of this medicine, ask your doctor, pharmacist or nurse.

#### **4. POSSIBLE SIDE EFFECTS**

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Side effects related to the first infusion are very common (occurring in more than 30% of patients) but are less common following subsequent infusions. The majority of the side effects, such as fever and chills, pain in the muscles or joints, and headache, occur within the first three days following the dose of Zoledronic Acid. The symptoms are usually mild to moderate and go away within three days. Your doctor can recommend a mild pain reliever such as ibuprofen or paracetamol to reduce these side effects. The chance of experiencing these side effects decreases with subsequent doses of Zoledronic Acid.

Some side effects could be serious.

##### Common (may affect up to 1 in 10 people)

Irregular heart rhythm (atrial fibrillation) has been seen in patients receiving Zoledronic Acid for the treatment of 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.

Swelling and/or pain at the infusion site may occur.

##### Uncommon (may affect up to 1 in 100 people)

Skin reactions such as redness.

Swelling, redness, pain and itching to the eyes or eye sensitivity to light.

##### Not known (frequency cannot be estimated from the available data)

Pain in the mouth, teeth and jaw, swelling or sores inside the mouth, 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 dentist immediately if you experience such symptoms.

Kidney disorders (e.g. decreased urine output) may occur. Your doctor should do a blood test to check your kidney function before each dose of Zoledronic Acid. It is important for you to drink at least 2 glasses of fluid (such as water), within a few hours before receiving Zoledronic Acid, as directed by your healthcare provider.

##### Very rare

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.

If you experience any of the above side effects, you should contact your doctor immediately.

#### **Zoledronic Acid may also cause other side effects**

##### Very common (may affect more than 1 in 10 people)

Fever

##### Common (may affect up to 1 in 10 people)

Headache, dizziness, sickness, vomiting, diarrhoea, pain in the muscles, pain in the bones and/or joints, pain in the back, arms or legs, flu-like symptoms (e.g. tiredness, chills, joint and muscle pain), chills, feeling of tiredness and lack of interest, weakness, pain, feeling unwell.

In patients with Paget's disease, symptoms due to low blood calcium, such as muscle spasms, or numbness, or a tingling sensation especially in the area around the mouth have been reported.

Uncommon (may affect up to 1 in 100 people)

Flu, upper respiratory tract infections, decreased red cell count, loss of appetite, sleeplessness, sleepiness which may include reduced alertness and awareness, tingling sensation or numbness, extreme tiredness, trembling, temporary loss of consciousness, eye infection or irritation or inflammation with pain and redness, spinning sensation, increased blood pressure, flushing, cough, shortness of breath, upset stomach, abdominal pain, constipation, dry mouth, heartburn, skin rash, excessive sweating, itching, skin reddening, neck pain, stiffness in muscles, bones and/or joints, joint swelling, muscle spasms, shoulder pain, pain in your chest muscles and rib cage, joint inflammation, muscular weakness, abnormal kidney test results, abnormal frequent urination, swelling of hands, ankles or feet, thirst, toothache, taste disturbances.

Rare (may affect up to 1 in 1,000 people)

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.

Not known (frequency cannot be estimated from the available data)

Severe allergic reactions including dizziness and difficulty breathing, swelling mainly of the face and throat, decreased blood pressure, dehydration secondary to post-dose symptoms such as fever, vomiting and diarrhoea.

**Reporting of side effects**

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. Also, you can help make sure medicines remain as safe as possible by reporting any unwanted side-effects via the internet at [www.mhra.gov.uk/yellowcard](http://www.mhra.gov.uk/yellowcard). Alternatively you can call Freephone 0808 100 3352 (available between 10am-2pm Monday – Friday) or fill in a paper form available from your local pharmacy. By reporting side effects, you can help provide more information on the safety of this medicine.

**5. HOW TO STORE ZOLEDRONIC ACID**

Your doctor, pharmacist or nurse knows how to store Zoledronic Acid properly.

- Keep this medicine out of the sight and reach of children.
- Do not use this medicine after the expiry date which is stated on the carton and vial after EXP. The expiry date refers to the last day of that month.
- The unopened vial does not require any special storage conditions.
- After opening:  
Chemical and physical stability has been demonstrated for 24 hours at 2°C - 8°C and at 25°C.

From a microbiological point of view, the solution for infusion should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at

2°C – 8°C. The refrigerated solution should then be equilibrated to room temperature prior to administration.

- Do not throw away any medicines via wastewater. 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 contains**

- The active substance is zoledronic acid. Each vial with 100 ml of solution contains 5 mg of zoledronic acid (as monohydrate).  
One ml solution contains 0.05 mg of zoledronic acid anhydrous (as monohydrate).
- The other ingredients are mannitol (E421), sodium citrate (E331) and water for injections.

### **What Zoledronic Acid looks like and contents of the pack**

Zoledronic Acid is a clear and colourless solution.

It comes in 100 ml clear Type I silicon dioxide inner coated glass vials, or alternatively in 100 ml Type II soda lime silica glass vials, capped with Type I bromobutyl rubber stoppers and sealed with aluminum polypropylene flip off seals, as a ready-to-use solution for infusion.

Zoledronic Acid 5mg/100ml solution for infusions is supplied in:

1 vial  
4 vials

Not all pack sizes may be marketed.

### **Marketing Authorisation Holder and Manufacturer**

#### **The Marketing Authorisation Holder is:**

Seacross Pharmaceuticals Limited,  
Bedford Business Centre  
61-63 St Peters Street  
Bedford, MK 40 2PR,  
UK

#### **The Manufacturer is:<sup>1</sup>**

Seacross Pharmaceuticals Ltd.  
Stanmore Place,  
Howard Road,  
Stanmore  
HA7 1BT  
UK

or,

Sanochemia Pharmazeutica AG, Landeggerstrasse 7, 2491 Neufeld an der Leitha, Austria.

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

**Denmark:** Zoledronsyre Seacross

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<sup>1</sup> Only the real batch release site will appear on the patient leaflet mockup.

**Germany:** Zoledronsäure Seacross 5mg/100ml Infusionslösung  
**Netherlands:** Zoledroninezuur Seacross 5mg/100ml, oplossing voor infusie  
**Norway:** Zoledronsyre Seacross  
**United Kingdom:** Zoledronic Acid 5mg/100 ml solution for infusion

**This leaflet was last approved in 03.11.2017**

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### **Information for the healthcare professional:**

**The following information is intended for medical or healthcare professionals only (see section 3):**

#### **How to prepare and administer Zoledronic Acid**

Zoledronic Acid 5 mg/100 ml solution for infusion is ready for use.

For single use only. Any unused solution should be discarded. Only clear solution free from particles and discoloration should be used. Zoledronic Acid must not be mixed or given intravenously with any other medicinal product and must be given through a separate vented infusion line at a constant infusion rate. The infusion time must not be less than 15 minutes. Zoledronic Acid must not be allowed to come into contact with any calcium-containing solutions. If refrigerated, allow the refrigerated solution to reach room temperature before administration. Aseptic techniques must be followed during preparation of the infusion. The infusion must be conducted according to standard medical practice.

#### **How to store Zoledronic Acid**

- Keep this medicine out of the sight and reach of children.
- Do not use this medicine after the expiry date which is stated on the carton and vial after EXP.
- The unopened vial does not require any special storage conditions.

After opening the vial, the product should be used immediately in order to avoid microbial contamination. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2°C - 8°C. Allow the refrigerated solution to reach room temperature before administration.