PACKAGE LEAFLET: INFORMATION FOR THE USER

Zoledronic Acid LOGENEX 4mg/5ml 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, 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.

What is in this leaflet:

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

1. WHAT ZOLEDRONIC ACID LOGENEX 4 MG/5 ML IS AND WHAT IT IS USED FOR

The active substance in Zoledronic Acid LOGENEX 4 mg/5 ml 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 LOGENEX 4 MG/5 ML

Follow carefully all instructions given to you by your doctor.

Your doctor will carry out blood tests before you start treatment with Zoledronic Acid LOGENEX 4 mg/5 ml and will check your response to treatment at regular intervals.

You should not be given Zoledronic Acid LOGENEX 4 mg/5 ml:
- if you are allergic (hypersensitive) to zoledronic acid, another bisphosphonate (the group of substances to which zoledronic acid LOGENEX belongs), or any of the other ingredients of this medicine (listed in section 6.)
- if you are breast-feeding.

Warnings and precautions:
- 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.
- if you are having **dental treatment** or are due to undergo dental surgery, tell your dentist that you are being treated with Zoledronic Acid LOGENEX 4 mg/5 ml.

Patients aged 65 years and over
Zoledronic Acid LOGENEX 4 mg/5 ml 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 LOGENEX 4 mg/5 ml is not recommended for use in adolescents and children below the age of 18 years.

Other medicines and Zoledronic Acid LOGENEX 4 mg/5ml
Please tell your doctor if you are taking or have recently taken any other medicines, including medicines obtained without a prescription. It is especially important that you tell your doctor if you are also taking:
- Aminoglycosides (medicines used to treat severe infections), 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.
- Zoledronic Acid LOGENEX contains the same active substance as found in medicinal products indicated for treatment of osteoporosis and Paget's disease of the bone. Patients being treated with Zoledronic Acid LOGENEX should not be treated with such products concomitantly since the combined effects of these agents are unknown.
- Anti-angiogenic medicines (used to treat cancer), since the combination of these with zoledronic acid has been associated with reports of osteonecrosis of the jaw (ONJ).

Pregnancy and breast-feeding
You should not be given Zoledronic Acid LOGENEX 4 mg/5 ml if you are pregnant. Tell your doctor if you are or think that you may be pregnant.
You must not be given Zoledronic Acid LOGENEX 4 mg/5 ml 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 LOGENEX 4 mg/5 ml. You should therefore be careful when driving, using machinery or performing other tasks that need full attention.

Zoledronic acid LOGENEX 4mg/5ml contains Sodium
This medicinal product contains less than 1 mmol sodium (23 mg) per vial., i. e. essentially 'sodium-free'

3. HOW ZOLEDRONIC ACID LOGENEX 4 MG/5 ML IS USED

Zoledronic Acid LOGENEX 4 mg/5 ml 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 LOGENEX 4 mg/5 ml 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 an the severity of your kidney problem.

How often Zoledronic Acid LOGENEX 4 mg/5 ml 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 LOGENEX 4 mg/5 ml 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 LOGENEX 4 mg/5 ml.

How Zoledronic Acid LOGENEX 4 mg/5 ml is given
- Zoledronic Acid LOGENEX 4 mg/5 ml is given as a drip (infusion) into a vein which should take of 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 LOGENEX 4 mg/5 ml 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, Zoledronic Acid LOGENEX 4 mg/5 ml 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 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 doctor and dentist immediately if you experience such symptoms.
- 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.
- Severe allergic reaction: shortness of breath, swelling mainly of the face and throat.

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, pain, 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, sleep disturbances, tingling or numbness of the hands or feet, diarrhoea.
- 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.
- Sleepiness.
- 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 1000 people):
- Slow heart beat.
- Confusion.
- Unusual fracture of the thigh bone particularly in patients an 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.

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.
- Painful redness and/or swelling of the eye.

If you get any side effects, talk to your doctor, nurse or pharmacist. This includes any possible side effects not listed in this leaflet.

5. HOW TO STORE ZOLEDRONIC ACID LOGENEX 4 MG/5 ML

Keep Zoledronic Acid LOGENEX 4 mg/5 ml out of the sight and reach of children

Do not use Zoledronic Acid LOGENEX 4 mg/5 ml after the expiry date which is stated on the pack. The expiry date refers to the last day of that month.

The unopened vial does not require any specific storage conditions.

The readily prepared Zoledronic Acid LOGENEX4 mg/5 ml infusion solution should preferably be used immediately in order to avoid microbial contamination. If the solution is not used immediately, storage prior to use is the responsibility of the user and should be in a refrigerator at 2°C – 8°C.

The total time between dilution, storage in the refrigerator and end of administration must not exceed 24 hours.

Chemical and physical in-use stability has been demonstrated for 24 hours at 2°C- 8°C when diluted with 100ml of physiological saline or 5%w/v glucose.

6. CONTENTS OF THE PACK AND OTHER INFORMATION

What Zoledronic Acid LOGENEX 4 mg/5 ml contains

Each vial with 5 ml concentrate contains 4 mg zoledronic acid (as monohydrate, corresponding to 4.264 mg zoledronic acid monohydrate). One ml concentrate contains 0.8 mg zoledronic acid (as monohydrate). The other ingredients are: mannitol (E421), sodium citrate (E331), water for injections.

What Zoledronic Acid LOGENEX 4 mg/5 ml looks like and contents of the pack

Zoledronic Acid LOGENEX 4 mg/5 ml is supplied as a clear and colourless liquid concentrate for solution for infusion in a vial.

Each pack contains the vial with concentrate. Zoledronic Acid LOGENEX 4 mg/5 ml is supplied as packs containing 1, 4 or 10 vials.
Not all pack sizes may be marketed.

Marketing Authorisation Holder

The Marketing Authorisation Holder is:
LOGENEX Pharm GmbH
Kleine Johannistrasse 10
20457 Hamburg
Germany

The Manufacturers are:

PharmIdea SIA
4 Rupnicu Str., Olaine
LV-2114
Latvia

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INFORMATION FOR THE HEALTHCARE PROFESSIONAL

How to prepare and administer Zoledronic Acid LOGENEX 4 mg/5 ml
- To prepare an infusion solution containing 4 mg zoledronic acid, further dilute the Zoledronic Acid LOGENEX 4 mg/5 mlconcentrate (5.0 ml) with 100 ml of calcium-free or other divalent cation-free infusion solution. If a lower dose of Zoledronic Acid LOGENEX 4 mg/5 ml 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 LOGENEX 4 mg/5 ml concentrate with calcium-containing or other divalent cation¬containing solutions such as lactated Ringer's solution.

Instructions for preparing reduced doses of Zoledronic Acid LOGENEX 4 mg/5 ml:
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.
- From a microbiological point of view, the diluted 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.
- The solution containing zoledronic acid is given as a single 15-minute intravenous infusion in a separate infusion line. The hydration status of patients must be assessed prior to and following administration of Zoledronic Acid LOGENEX 4 mg/5 ml to ensure that they are adequately hydrated.
- Studies several types of infusion lines made from polyvinylchloride, polyethylene and
- polypropylene showed no incompatibility with Zoledronic Acid LOGENEX 4 mg/5 ml.
- Since no data are available on the compatibility of Zoledronic Acid LOGENEX 4 mg/5 ml with other intravenouslyadministered substances, Zoledronic Acid LOGENEX 4 mg/5 ml must not be mixed with other medications/substances and should always be given through a separate infusion line.

How to store Zoledronic Acid LOGENEX 4 mg/5 ml
- Keep Zoledronic Acid LOGENEX4 mg/5 ml out of the reach and sight of children.
- Do not use Zoledronic Acid LOGENEX4 mg/5 ml after the expiry date stated on the pack.
- The unopened vial does not require any specific storage conditions.
- The diluted Zoledronic Acid LOGENEX 4 mg/5 ml infusion solution should be used immediately in order to avoid microbial contamination.