Artwerk creative designs
Artwork at upshot
e-mail : artwerkcd@gmail.com
prasad.pdp@gmail.com
Ph : +91-9845156610

Colours Used: Black

Keyline | Unvarnish area

Artwork No.	110121/2
Customer	Ennogen
Description	Zolendronic Acid Leaflet
Market	UK
Language	English
Dimensions	190 x 370 mm
Min. Font Size	Swis721 cn bt, 9.5 pt
Version No.	3
Date	20-12-21

Pharmacode

Ennogen Healthcare

Package leaflet: Information for the user

Zoledronic Acid Ennogen 4 mg/5 ml concentrate for solution for infusion

Zoledronic acid monohydrate

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

1. What Zoledronic Acid Ennogen is and what it is used for

The active substance in Zoledronic Acid Ennogen is zoledronic acid monohydrate, which belongs to a group of substances called bisphosphonates. Zoledronic acid monohydrate 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 Ennogen

Follow carefully all instructions given to you by your doctor.
- Your doctor will carry out **blood tests** before you start treatment with Zoledronic Acid Ennogen and will check your response to treatment at regular intervals.
- Your doctor will recommend that you **drink enough water** before each treatment to help prevent dehydration.

Do not take Zoledronic Acid Ennogen:
- if you are breast-feeding.
- if you are allergic to zoledronic acid monohydrate, another bisphosphonate (the group of substances to which Zoledronic Acid Ennogen 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 Ennogen:
- 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 Ennogen.
- if you are having **dental treatment** or are due to undergo dental surgery, tell your dentist that you are being treated with Zoledronic Acid Ennogen and inform your doctor about your dental treatment.

While being treated with Zoledronic Acid Ennogen, you should maintain good oral hygiene (including regular teeth brushing) and receive routine dental check-ups.

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.**

If you have pre-existing **hypocalcaemia** (reduced levels of calcium in the blood), it must be corrected before you receive the first dose of Zoledronic Acid Ennogen. You will be given adequate calcium and vitamin D supplements. Reduced levels of calcium in the blood sometimes lead to muscle cramps, dry skin, burning sensation, irregular heart beat, seizures, spasm and twitching. In some instances, hypocalcaemia may be life-threatening.

Patients aged 65 years and over
Zoledronic Acid Ennogen 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 Ennogen is not recommended for use in adolescents and children below the age of 18 years.

Other medicines and Zoledronic Acid Ennogen
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.
- **Aclasta** (a medicine that also contains zoledronic acid and is 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 Ennogen are unknown.
- **Certain medicines to treat cancer** (anti-angiogenic medicines), since the combination of these with Zoledronic Acid Ennogen has been associated with an increased risk of osteonecrosis of the jaw.

Pregnancy, breast-feeding and fertility
You should not be given Zoledronic Acid Ennogen if you are pregnant. Tell your doctor if you are or think that you maybe pregnant.
You must not be given Zoledronic Acid Ennogen if you are breast-feeding.
Ask your doctor for advice before taking any 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 Ennogen. You should avoid driving or using machinery if you feel drowsy or sleepy.

Zoledronic Acid Ennogen contains sodium
This medicinal product contains less than 1 mmol sodium (23 mg) per vial (5 ml),that is to say essentially “sodium-free”.

3. How Zoledronic Acid Ennogen is used

- Zoledronic Acid Ennogen must only be given by healthcare professionals trained in administering bisphosphonates intravenously, i.e. through a vein.
- Carefully follow all the other instructions given to you by your doctor, pharmacist or nurse.

How much Zoledronic Acid Ennogen 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 Ennogen 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 Ennogen 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 Ennogen.

How Zoledronic Acid Ennogen is given
- Zoledronic Acid Ennogen 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 Ennogen than you should be
If you have received doses higher than those recommended, you will be carefully monitored by your doctor. This is because you may develop abnormal levels of calcium, phosphorus and magnesium in your blood and/or changes in kidney function, including severe kidney problems. 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.

Serious side effects - tell your doctor immediately about any of the following serious side effects:
- **Severe kidney impairment** (will normally be determined by your doctor with certain specific blood tests); (common: may affect up to 1 in 10 people).
- **Low level of calcium** in the blood; (common: may affect up to 1 in 10 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 Ennogen or after stopping treatment; (uncommon: may affect up to 1 in 100 people).
- **Irregular heart rhythm** (atrial fibrillation); (uncommon: may affect up to 1 in 100 people).
- Severe allergic reaction: **shortness of breath, swelling mainly of the face and throat;** (uncommon: may affect up to 1 in 100 people).
- **Irregular heart beat** (rare: may affect up to 1 in 1,000 people).
- **A kidney function disorder** called Fanconi syndrome (will normally be determined by your doctor with certain urine tests); (rare: may affect up to 1 in 1,000 people).
- **Seizures, numbness and twitching** (very rare: may affect up to 1 in 10,000 people).
- **Ear pain, discharge from the ear,** and/or an **ear infection**. These could be signs of bone damage in the ear; (very rare: may affect up to 1 in 10,000 people).
- **Osteonecrosis of the hip or thigh,** such as new onset or worsening of aches, pain or stiffness (very rare: may affect up to 1 in 10,000 people).

Other side effects - tell your doctor about any of the following side effects:

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 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):
- Allergic 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.
- Low counts of white blood cells and blood platelets (seen in a blood test).
- Low level of magnesium and potassium in the blood. Your doctor will monitor this and take any necessary measures.
- Weight increase.
- Increased sweating.
- 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 (nettle rash).

Rare (may affect up to 1 in 1,000 people):
- Slow heart beat.
- 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, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the Yellow Card Scheme at Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Zoledronic Acid Ennogen

This medicinal product does not require any special storage conditions.
After dilution: 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.
Your doctor, pharmacist or nurse knows how to store Zoledronic Acid Ennogen properly (see section 6).

6. Contents of the pack and other information

What Zoledronic Acid Ennogen contains
- The active substance of Zoledronic Acid Ennogen is zoledronic acid monohydrate. One vial contains 4 mg zoledronic acid, corresponding to 4.264 mg zoledronic acid monohydrate.
- The other ingredients are: mannitol, sodium citrate, water for injections.

What Zoledronic Acid Ennogen looks like and contents of the pack
Zoledronic Acid Ennogen is supplied as a liquid concentrate in a vial. It is a clear and colourless solution, practically free from visible particles. One vial contains 4 mg of zoledronic acid.

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

Marketing Authorisation Holder & Manufacturer
Ennogen Healthcare Ltd,
Unit G2-G4,
Riverside Industrial Estate,
Riverside Way, Dartford,
DA1 5BS, United Kingdom.

This leaflet was last revised in December 2021

ENV02

Perforation

INFORMATION FOR THE HEALTHCARE PROFESSIONAL

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

Instructions for preparing reduced doses of Zoledronic Acid Ennogen:
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 monohydrate 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 Ennogen to ensure that they are adequately hydrated.

Studies with several types of infusion lines made from polyvinylchloride, polyethylene and polypropylene showed no incompatibility with Zoledronic Acid Ennogen.

Since no data are available on the compatibility of Zoledronic Acid Ennogen with other intravenously administered substances, Zoledronic Acid Ennogen must not be mixed with other medications/substances and should always be given through a separate infusion line.

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

Date of revision: December 2021.

370 mm
190 mm