ZOLEDRA 4 MG
INN : Zoledronic acid
Powder for solution for infusion

Read all of this leaflet carefully before you start taking this medicine.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if their symptoms are the same as yours.
- If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

In this leaflet:

1. What's Zoledra 4 mg is and in which cases it is used for?
- Treatment of patients with bone metastases from solid tumors and multiple myeloma in combination with standard antineoplastic therapy.
- Treatment of hypercalcemia of malignancy (HCM).

2. What you need to know before taking Zoledra 4 mg?
Follow carefully all instructions given to you by your doctor.
Your doctor will carry out blood tests before you start treatment with Zoledra 4 mg and will check your response to treatment at regular intervals.

Do not use Zoledra 4 mg
- if you are breast-feeding.
- if you are allergic to zoledronic acid, another bisphosphonate (the group of substances to which Zoledra 4mg/5ml belongs), or any of the other ingredients of this medicine.

Take special care with Zoledra 4 mg
Talk to your doctor before receiving Zoledra:
- 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 Zoledra 4 mg.

Reduced levels of calcium in the blood (hypocalcaemia), sometimes leading to muscle cramps, dry skin, burning sensation, have been reported in patients treated with Zoledra 4 mg. 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.

Patients aged 65 years and over
Zoledra 4 mg 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
Zoledra 4 mg is not recommended for use in adolescents and children below the age of 18 years.

Using other medicines and Zoledra 4 mg :
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.
– 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 Zoledra 4 mg are unknown.
– Anti-angiogenic medicines (used to treat cancer), since the combination of these with Zoledra 4 mg has been associated with an increased risk of osteonecrosis of the jaw (ONJ).
Please tell your doctor, health care provider or pharmacist if you are taking or have recently taken any other medecines, including medecines obtained without a prescription.

Pregnancy and breast-feeding :
You should not be given Zoledra 4 mg if you are pregnant. Tell your doctor if you are or think that you may be pregnant.
You must not be given Zoledra 4 mg if you are breast-feeding.
Ask your doctor, health care provider or pharmacist for advice before taking any medicine.

Driving and using machines :
It has been observed very rare cases of drowsiness and sleepiness with Zoledra 4 mg.
Caution is advised when driving vehicles, operating machinery or when performing other tasks that require your attention.

3. How you take Zoledra 4 mg ?
Zoledra 4 mg 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, pharmacist or nurse.

How much Zoledra 4 mg 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 Zoledra 4 mg is given ?
– If you are being treated for the prevention of bone complications due to bone metastases, you will be given one infusion of Zoledra 4 mg 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 Zoledra 4 mg.

How Zoledra 4 mg is given
– Zoledra 4 mg 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 Zoledra 4 mg than you should:
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. What are the 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 determ ined 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.

Very rare (may affect up to 1 in 10,000 people):
- As a consequence of low calcium values: irregular heart beat (cardiac arrhythmia; secondary to hypocalcaemia), seizures, numbness and tetany (secondary to hypocalcaemia).

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, 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 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.

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 any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor, health care provider or pharmacist.

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.

5. How to store Zoledra 4 mg
Keep out of the reach and sight of children.
- No special storage.
- Do not use Zoledra 4 mg after the expiry date stated on the box.
- The unopened vial does not require any special storage conditions.

6. Further information
a- What Zoledra 4 mg contains:

	Zoledra 4 mg
Actif ingredient :	
Zoledronic acid (as zoledronic acid monohydrate)	4 mg (4.264 mg)
Excipients :	
Mannitol, trisodium citrate	s.q.

b- What Zoledra 4 mg looks like and contents of the pack:
Zoledra 4 mg – INN : Zoledronic acid – powder for solution ofr infusion – Box of one vial – M.A. N°: 923 370 1H

c- Marketing Authorization Holder and Manufacturer:
LES LABORATOIRES MEDIS- S.A.
Route de Tunis - KM 7 - BP 206 - 8000 Nabeul - Tunisie
Tel: (216) 72 23 50 06
Fax: (216) 72 23 51 06
E-mail: marketing.ventes@medis.com.tn

d- Date of the last revision of this leaflet : December 2014

INFORMATION FOR THE HEALTHCARE PROFESSIONAL
How to prepare and administer Zoledra 4 mg
• To prepare an infusion solution containing 4 mg zoledronic acid, add 5 ml of water for injections from the ampoule supplied in the pack to the vial containing the Zoledra 4 mg powder under aseptic conditions. Shake the vial gently to dissolve the powder.
• Further dilute the Zoledra 4 mg reconstituted solution (5 ml) with 100 ml of calcium-free or other divalent cation-free infusion solution. If a lower dose of Zoledra 4 mg is required, first withdraw the appropriate volume of the reconstituted solution (4 mg/5 ml) 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 Zoledra 4 mg reconstituted solution with calcium-containing or other divalent cation-containing solutions such as lactated Ringer's solution.
Instructions for preparing reduced doses of Zoledra 4 mg:
Withdraw the appropriate volume of the reconstituted solution (4 mg/5 ml), 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 reconstituted and 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 Zoledra 4 mg to assure that they are adequately hydrated.
• Studies with several types of infusion lines made from polyvinylchloride, polyethylene and polypropylene showed no incompatibility with Zoledra 4 mg.
• Since no data are available on the compatibility of Zoledra 4 mg with other intravenously administered substances, Zoledra 4 mg must not be mixed with other medications/substances and should always be given through a separate infusion line.
- How to store Zoledra 4 mg
- Keep out of the reach and sight of children.

• Do not use Zoledra 4 mg after the expiry date stated on the pack.
• The unopened vial does not require any specific storage conditions.
• The diluted Zoledra 4 mg infusion solution should be used immediately in order to avoid microbial contamination.

THIS IS A DRUG
- A drug is a product but not like the others.
- A drug is a product that is on your health and its non-conformity with the requirements consumption exposes you to danger.
- Follow strictly the doctor's prescription and the instructions that tells you to follow the advice of your pharmacist.
- Your doctor and pharmacist know about the drug, its indications and cons-indications.
- Do not stop your own treatment during the prescribed period.
- Do not pick up, do not increase the dose without consulting your doctor.

KEEP ANY DRUG OUT OF THE REACH OF CHILDREN.

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