# Zoledra® 4mg, 4 mg/5 ml
## Powder for injection
Zoledronic Acid

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

**What is in this leaflet?**


**1.What is Zoledra 4mg and in which case is it used?**
The active substance contained in Zoledra 4mg is the zoledronic acid that belongs to a group of substances called bisphosphonates. The zoledronic acid works by attaching to the bone and slowing down the rate of bone turnover. It is used:
•**To prevent bone complications,** ex. fractures, in adult patients bone Metastases (spread of cancer from the primary site to the bone).
•**To decrease calcium level** in the blood in adult patients when it is high because of the presence of the tumor. Tumors can accelerate the usual bone turnover and cause the increase of the amount of bone released calcium. This pathology is called tumor-induced hypercalcemia.

**2.What you need to know before you take Zoledra 4mg?**
Carefully follow all the instructions of your doctor.
Your doctor may perform blood tests before Zoledra 4mg intake is started and may check your response to the treatment at regular intervals.
**You should not take Zoledra 4mg:**
-If you are currently breastfeeding.
- If you are allergic to zoledronic acid, to any other bisphosphonate (the substance group to which Zoledra 4mg belongs) or to one of the other components contained in this medicine (mentioned in section 6).
**Warnings and precautions**
**Talk to your doctor before you receive Zoledra 4mg:**
-if you have or have had a **kidney** problem.
-if you have or have had **pain, swelling, numbness** or a feeling of heaviness in the jaw or a loosened tooth. Your doctor may recommend that you have a dental examination before you start Zoledra 4mg treatment
-if you are currently having **dental care** or if you are undergoing dental surgery,
Tell your doctor that you are being treated with Zoledra 4mg and tell your doctor about your dental care.
During your treatment with Zoledra 4mg, you must maintain good oral hygiene (including regular brushing of teeth) and regular dental checkups.
Contact your doctor and dentist immediately if you experience problems with your mouth or teeth such as loose teeth, pain or swelling, or non-healing of wounds or discharge, as these may be signs of a disorder called osteonecrosis of the jaw.
Patients on chemotherapy and / or radiotherapy, who are taking corticosteroids, who are undergoing dental surgery, who do not receive regular dental care, who have gum disease, who are smokers or who have previously been treated with a bisphosphonate (used to treat or prevent bone disorders) may present a higher risk of developing osteonecrosis of the jaw.
A decrease in the level of calcium in the blood (hypocalcemia), sometimes causing muscle cramps, dryness of the skin, burning sensations have been reported in patients treated with Zoledra 4mg. Irregular heart beat (cardiac arrhythmia), seizures, spasms and contractions (tetany) have been reported secondarily to severe hypocalcemia. In some cases, hypocalcemia can be life-threatening. If you have any of these signs, tell your doctor immediately. If you have hypocalcemia, it should be cured before starting treatment with Zoledra 4mg. Appropriate calcium and vitamin D supplements will be prescribed.
**Patients aged 65 and over**
Zoledra can be given to patients aged 65 and over. There is no indication that additional precautions are needed.
**Children and adolescents**
Zoledra 4mg is not recommended in adolescents and children under 18 years old.
**Other medicines and Zoledra 4mg**
Tell your doctor if you are taking, have recently taken or might take any other medicines. It is particularly important that your doctor knows if you are also taking:
-aminoglycosides (a family of medicines used to treat severe infections), calcitonin (a type of medicine used to treat postmenopausal osteoporosis and hypercalcemia), loop diuretics (a type of medicine used to treat high blood pressure or edema) or other calcium-lowering medicines, since the combination of these with bisphosphonates can lead to a sharp decrease of calcium in the blood.
-Thalidomide (a medicine used to treat some blood cancer with bone disorders) or any other medicine that can damage your kidneys.
-Aclasta (a medicine that also contains zoledronic acid and is used to treat osteoporosis and other non-cancerous bone diseases), or any other bisphosphonate, as the effects of these combinations are unknown.
-Anti-angiogenic medicines (used to treat cancer) because an increased risk of osteonecrosis of the jaw (ONJ) has been associated with concomitant use of these medications with Zoledra 4mg.
**Pregnancy and breastfeeding**
You should not take Zoledra 4mg if you are pregnant. Tell your doctor if you are or think you are pregnant.
You should not take Zoledra 4mg if you are breastfeeding. Ask your doctor for advice before taking any medicine if you are pregnant or breastfeeding.
**Driving and using machines**
Very few cases of drowsiness and sleep have been observed with Zoledra 4mg. Caution is advised when driving vehicles, using machines, or performing other tasks that require your full attention.

**3.How to take Zoledra 4mg?**
-Zoledra 4mg should only be administered by healthcare professionals who are experienced in the administration of intravenous bisphosphonates i.e. into a vein.
-Your doctor will advise you to drink enough water before each administration to prevent dehydration.
-Carefully follow all other instructions given by your doctor, pharmacist or nurse.
**How much Zoledra 4mg is administered**
-The usual administered single dose is 4mg.
-If you have a kidney problem, your doctor will give you a lower dose depending on the severity of your kidney problem.
**How many times is Zoledra 4mg administered?**
-If you are being treated for the prevention of bone complications related to bone metastases, Zoledra 4mg will be given as an infusion every 3 to 4 weeks.
- If you are treated to reduce the level of calcium in your blood, you will normally receive only one infusion of Zoledra 4mg.
**How is Zoledra 4mg administered?**
-Zoledra 4mg is administered as a slow intravenous infusion which should last at least 15 minutes and should be administered as a single intravenous infusion.
Patients with low calcium levels will receive additional daily calcium and vitamin D supplementation.
**If you have taken more Zoledra 4mg than you should**
If you have received higher doses than recommended, you should be closely monitored by your doctor. In fact, you may develop serum electrolyte abnormalities (eg, abnormal levels of calcium, phosphorus, and magnesium) and / or changes in kidney function, including severe kidney failure. If your calcium level drops too low, you should receive infusions of calcium supplements.

**4.Possible side effects?**
Like any medicine, this medicine may cause side effects, but not everybody gets them. The most common are usually moderate and will probably disappear after a short period of time.
**Tell your doctor immediately if any of the following serious side effects occur:**
**Common (can affect up to 1 in 10 people):**
-Severe renal impairment (which will generally be determined by your doctor with blood tests).
-Low calcium levels in the blood.
**Uncommon (may affect up to 1 in 100 people):**
-Pain in the mouth, teeth and / or jaw, swelling or unhealed wounds in the mouth or jaw, discharge, numbness or feeling of heaviness in the jaw, or moving of a tooth. These symptoms could be signs of bone damage of the jaw (osteonecrosis). Tell your doctor and dentist immediately if you have any of these symptoms while taking Zoledra 4mg or after stopping treatment.
-Irregular heart rhythm (atrial fibrillation) has been observed in patients receiving zoledronic acid for the treatment of postmenopausal osteoporosis. It has not been clearly proven that zoledronic acid causes these abnormal heart rhythms but if these symptoms occur after you have received zoledronic acid you should tell your doctor.
-Severe allergic reaction: shortness of breath, swelling mainly of the face and throat.
**Rare (may affect up to 1 in 1000 people):**
-As a result of low calcium level: irregular heartbeat (cardiac arrhythmia, secondary to hypocalcemia).
-A kidney function disorder called Fanconi syndrome (which will usually be diagnosed by your doctor through urine tests).
**very rare (may affect up to 1 in 10000 people):**
-As a result of low calcium level: convulsions, numbness and tetany (secondary to hypocalcemia).
-Consult your doctor if you have ear pain, ear discharge, and / or ear infection. It could be signs of bone damage to the ear.
-Osteonecrosis of other bones than the jawbone was very rarely observed and mainly affected the hip or thigh (femur). Tell your doctor immediately if you experience any symptoms such as developing or worsening pain or stiffness while taking Zoledra 4mg or after stopping treatment.
**Tell your doctor as soon as possible if any of the following side effects occur:**
**Very common (may affect more than 1 in 10 people):**
-Low level of phosphates in the blood.
**common (may affect up to 1 in 10 people):**
-Headache and flu-like illness manifesting as fever, fatigue, weakness, drowsiness, chills and pain in the bones, joints and / or muscles. In most cases, no specific treatment is required and the symptoms disappear quickly (in a few hours or days).
-Gastrointestinal reactions such as nausea, vomiting and loss of appetite.
-Cases of conjunctivitis.
-Low red blood cell count (anemia).
**Uncommon (may affect up to 1 in 100 people):**
-Hypersensitivity reactions.
-low blood pressure.
-chest pain.
-Skin reactions (redness or swelling) at the injection site, rash, itching.
-high blood pressure, shortness of breath, dizziness, anxiety, sleep disturbances, taste disturbances, tremors, tingling or numbness of hands or feet, diarrhea, constipation, abdominal pain, dry mouth.
-Decrease in the number of white blood cells and blood platelets.
-Low levels of magnesium and potassium in the blood. Your doctor will check them and take the necessary action.
-Weight gain.
-Increased sweating.
-Drowsiness.
-Blurred vision, tightness of the eye, sensitivity to light.
-Feeling of sudden cold with fainting, weakness and collapse.
-Difficulty breathing with coughing and gasp.
-hives.
**Rare (may affect up to 1 in 1000 people):**
-Slow heartbeat.
-Confusion.
-An unusual fracture of the thigh bone may infrequently occur, especially in long-term osteoporosis patients.
Contact your doctor if you experience pain, weakness or discomfort in the thigh, hip or groin as this may be an early sign of a possible fracture of the thigh bone.
-Interstitial pneumonitis (inflammation of the tissue surrounding the alveoli of the lungs).
-Flu-like symptoms with arthritis and joint swelling.
-Painful redness and / or swelling of the eye.
**Very rare (may affect up to 1 in 10000 people):**
-Fainting due to low blood pressure.
-Severe bone, joint and / or muscle pain, that may be disabling.
**Reporting of side effects**
If you get any side effects, talk to your doctor, pharmacist or nurse. This also applies to any side effects that are not mentioned in this leaflet. You can also report side effects directly via the national reporting system: CNPV (Centre National de Pharmacovigilance). By reporting side affects you can help provide more information on the safety of the medicine.

**5.How to store Zoledra 4mg?**
Your doctor, pharmacist or nurse know how to store Zoledra properly (see section 6).

**6.Content of the packaging and other information**
**what Zoledra 4mg contains**
-The active substance of Zoledra 4mg is zoledronic acid. One vial contains 4 mg of zoledronic acid corresponding to 4,264 mg of zoledronic acid monohydrate.
-the other components: mannitol, trisodium citrate, water for injections.
**What Zoledra 4mg looks like and content of the outer packaging**
Zoledra 4mg is in the form of a powder for injection in boxes of 1 vial.
Each vial contains 4mg of Zoledronic acid.
**Marketing Authorisation MAN°:** 9233701H
**Marketing Authorization Holder and Manufacturer**
LES LABORATOIRES MEDIS
Tunis road - KM 7 - BP 206 - 8000 Nabeul - Tunisia
Phone : (216) 72 23 50 06. Fax: (216) 72 23 50 16.
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**Supply and prescription conditions :** list I
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**INFORMATION FOR HEALTHCARE PROFESSIONALS**
**How to prepare and administer Zoledra 4mg**
-To prepare a solution for infusion containing 4 mg of zoledronic acid, dilute the solution of Zoledra 4 mg (5ml) in 100 ml of an infusion solution free of calcium or other divalent cations. If a lower dose is needed, first take the appropriate volume as indicated below and then dilute it in 100ml of solution for infusion. To avoid potential incompatibilities, the infusion solution used for dilution should be either 0.9% w / v sodium chloride or 5% w / v glucose solution.
**Do not mix Zoledra 4mg concentrate with solutions containing calcium or other divalent cations such as lactated Ringer's solution.**
Instructions for preparing reduced doses of Zoledra 4mg : Collect an appropriate volume of the concentrated solution as follows :
-4.4 ml for a dose of 3.5 mg
-4,1 ml for a dose of 3,3 mg
-3,8 ml for a dose of 3,0 mg
-Reserved for a single use. Any unused solution must be discarded. Only a clear, particle-free, colorless solution should be used. The preparation of the infusion must be performed under aseptic conditions.
-From a microbiological point of view, the diluted solution for infusion should be used immediately. If it is not used immediately, the duration and storage conditions before use are the responsibility of the user and must not exceed 24 hours at 2 ° C to 8 ° C. room temperature before administration.
-The solution containing zoledronic acid is administered in a single 15 minute infusion through a separate infusion line The hydration status of patients should be assessed before and after administration of Zoledra 4mg to ensure they are adequately hydrated.
- Studies with several types of polyvinyl chloride, polyethylene and polypropylene infusion tubing showed no incompatibility with Zoledra 4mg.
-Since no data is available on the compatibility of Zoledra 4mg with other intravenously administered substances, Zoledra 4mg should not be mixed with other medicines or substances and should always be given through a separate infusion line.
**How to store Zoledra 4mg ?**
-keep out of the reach and sight of children.
-Do not use Zoledra 4mg after the expiry date which is stated on the carton.
-Unopened vials do not require special storage precautions.
-After opening, the diluted infusion solution of Zoledra 4mg should be used immediately to prevent contamination.

**This is a medicine**
- A medicine is a product but not like any other product.
- A medicine is a product that affects your health.if it's not used properly : it can be health threatening.
- Strictly adhere to the prescription of you Doctor and the use instructions prescribed, follow your pharmacist advice.
- Your doctor and you pharmacist know the medicine, its use and side effect.
- Don't stop the use of the treatment on your own during the prescribed time.
- Don't retake, Don't increase the doses without doctor's advice.

**Keep the medicines out of reach of children**

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