**PATIENT PACKAGE INSERT IN ACCORDANCE WITH THE PHARMACISTS' REGULATIONS (PREPARATIONS) - 1986**

The medicine is dispensed with a doctor's prescription only

# Zomera 4 mg/5 ml

# Concentrate for solution for infusion

Zoledronic acid 4 mg in 5 ml vial

**Inactive and allergenic ingredients: see section 6 "Further information".**

**Read this leaflet carefully in its entirety before using the medicine.** This leaflet contains concise information about the medicine. If you have further questions, refer to the doctor or pharmacist.

This medicine has been prescribed to treat your ailment. Do not pass it on to others. It may harm them even if it seems to you that their ailment is similar.

## 1. WHAT IS THE MEDICINE INTENDED FOR?

Zomera is used to:

- treat patients with multiple myeloma and patients with documented bone metastases (spread of cancer from primary site to the bone), together with standard anticancer therapy.
  For prostate cancer, the treatment is given if there is progression after at least one hormonal treatment.
- reduce the amount of calcium in the blood in patients where the level is too high due to the presence of a tumour.

**Therapeutic group**

Bisphosphonates

The active substance in Zomera 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.

## 2. BEFORE USING THE MEDICINE

Carefully follow all the instructions given to you by the doctor.

**☒ Do not use the medicine if:**

- you are sensitive (allergic) to zoledronic acid, another bisphosphonate (the group of substances to which zoledronic acid belongs) or any of the other ingredients contained in the medicine (detailed in section 6, in the list of inactive ingredients).
- you are breast-feeding.

**Special warnings regarding use of the medicine**

**▯ Before treatment with Zomera, tell the doctor if:**

- you have or have had a kidney problem.
- 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 Zomera.
- you are having dental treatment or are due to undergo dental surgery; tell your dentist that you are being treated with Zomera and inform your doctor about your dental treatment.

**▯ While being treated with Zomera**

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

Refer to a doctor and dentist immediately if you experience any problems with your mouth or teeth such as loose teeth, pain or swelling, or non-healing or discharging sores, as these could be signs of a condition called osteonecrosis of the jaw.

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 problems, 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.

Reduced levels of calcium in the blood (hypocalcaemia), sometimes leading to muscle cramps, dry skin, burning sensation, have been reported in patients treated with Zomera. Irregular heart beat (cardiac arrhythmia), seizures, spasms and twitching (tetany) have been reported as secondary to severe hypocalcaemia. In some instances, the hypocalcaemia may be life-threatening. If any of the symptoms apply to you, tell your doctor immediately. If you have hypocalcaemia before treatment, it must be corrected before initiating treatment with Zomera. You will be given adequate calcium and vitamin D supplements.

**▯ Other medicines and Zomera**

**If you are taking, or have recently taken, other medicines, including non-prescription medicines and nutritional supplements, tell the doctor or pharmacist.** In particular, if you are taking:

- Aminoglycosides (medicines used to treat severe infections), calcitonin (a medicine used to treat postmenopausal osteoporosis and hypercalcaemia), loop diuretics (a medicine to treat high blood pressure or oedema) or other calcium-lowering medicines. The combination of these medicines 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 (an additional medicine that 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 are unknown.
- Anti-angiogenic medicines (used to treat cancer). The combination of these medicines with Zomera has been associated with an increased risk of osteonecrosis of the jaw.

**▯ Pregnancy and breast-feeding**

You should not be given Zomera if you are pregnant. Tell your doctor if you are or think that you may be pregnant.

You must not be given Zomera if you are breast-feeding.

**▯ Driving and using machines**

There have been cases of drowsiness and sleepiness with the use of Zomera. Therefore, caution must be exercised when driving, using machinery or performing other activities that require full attention.

**▯ Children and adolescents**

This medicine is not recommended for use in adolescents and children under 18 years of age.

**▯ Patients aged 65 years and over**

The medicine can be used for patients aged 65 years and older. There is no evidence to suggest that any extra precautions are needed.

**▯ Important information regarding some of the ingredients of the medicine**

Each vial (before dilution) contains 2.14 mg sodium.

## 3. HOW SHOULD YOU USE THE MEDICINE?

Always use according to the doctor's instructions. Check with the doctor or pharmacist if you are uncertain.

Zomera will only be given by a healthcare professional trained in administering bisphosphonates intravenously.

Your doctor will recommend that you drink enough water before each treatment to help prevent dehydration.

The dosage and treatment regimen will be determined by the doctor only.

**Do not exceed the recommended dose.**

**Tests and follow up:**

The doctor will perform blood tests before starting treatment with Zomera and will check your response to treatment at regular intervals.

**If you have received a higher dosage** than recommended, you must be carefully monitored by your doctor. This is because you may develop blood electrolyte abnormalities (e.g., abnormal levels of calcium, phosphorus and magnesium) and/or changes in kidney function, including severe kidney function impairment. If your blood level of calcium is too low, you may have to be given supplemental calcium by infusion.

Adhere to the treatment regimen as recommended by the doctor.

Even if there is an improvement in your health, do not stop treatment with the medicine without consulting the doctor.

Do not take medicines in the dark! Check the label and the dose each time you take the medicine. Wear glasses if you need them.

If you have further questions regarding use of the medicine, consult the doctor or pharmacist.

## 4. SIDE EFFECTS

As with any medicine, use of Zomera may cause side effects in some users. Do not be alarmed by the list of side effects. You may not suffer from any of them.

**Refer to a doctor immediately if you have one or more of the following severe side effects:**

**Common side effects (may affect up to 1 in 10 patients):**

- Severe kidney function impairment (will normally be determined by your doctor by specific blood tests).
- Low level of calcium in the blood.

**Uncommon side effects (may affect up to 1 in 100 patients):**

- 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 the doctor and dentist immediately if you experience these symptoms while being treated with Zomera or after stopping treatment.
- Irregular heart rhythm (atrial fibrillation) has been seen in patients receiving zoledronic acid for treatment of postmenopausal osteoporosis. It is unknown whether zoledronic acid causes irregular heart rhythm, but tell the doctor if you experience these symptoms while being treated with zoledronic acid.
- Severe allergic reaction: shortness of breath, swelling mainly of the face and throat.

**Rare side effects (may affect up to 1 in 1,000 patients):**

- As a consequence of low calcium levels: irregular heart beat (cardiac arrhythmia, secondary to hypocalcaemia).
- A kidney function disorder called Fanconi syndrome (will normally be determined by your doctor with certain urine tests).

**Very rare side effects (may affect up to 1 in 10,000 patients):**

- As a consequence of low calcium levels: seizures, numbness and tetany (secondary to hypocalcaemia).
- Tell 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.

**Refer to a doctor as soon as possible if you have one or more of the following side effects:**

**Very common side effects (may affect more than 1 in 10 patients):**

- Low level of phosphate in the blood.

**Common side effects (may affect up to 1 in 10 patients):**

- Headache and a flu-like syndrome, including 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 (a 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 side effects (may affect up to 1 in 100 patients):**

- 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, 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.
- Low level of magnesium and potassium in the blood. Your doctor will monitor this and act accordingly.
- 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.

**Rare side effects (may affect up to 1 in 1,000 patients):**

- Slow heart beat.
- Confusion.
- Unusual fracture of the thigh bone particularly in patients on long-term treatment for osteoporosis. Refer to the 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 sacs of the lungs).
- Flu-like symptoms including arthritis and joint swelling.
- Painful redness and/or swelling of the eye.

**Very rare side effects (may affect up to 1 in 10,000 patients):**

- Fainting due to low blood pressure.
- Severe bone, joint and/or muscle pain, occasionally incapacitating.

If a side effect occurs, if one of the side effects worsens or if you suffer from a side effect not mentioned in this leaflet, consult with the doctor.

Side effects can be reported to the Ministry of Health by clicking on the link "Report Side Effects of Drug Treatment" found on the Ministry of Health homepage (www.health.gov.il) that directs you to the online form for reporting side effects, or by entering the link: https://forms.gov.il/globaldata/getsequence/getsequence.aspx?formType=AdversEffectMedic@moh.gov.il

## 5. HOW SHOULD THE MEDICINE BE STORED?

- Avoid poisoning! This medicine, and any other medicine, should be kept in a safe place out of the reach of children and/or infants in order to avoid poisoning. Do not induce vomiting without explicit instruction from the doctor.
- Do not use the medicine after the expiry date (exp. date) that appears on the package. The expiry date refers to the last day of that month.
- Do not store above 30°C. Use the solution immediately after preparing it according to the instructions. If it is not used immediately, storage prior to use is the responsibility of the user and should be kept in a refrigerator (2-8°C). The cumulated time between preparing the solution, storage in the refrigerator and end of administration must be no longer than 24 hours.

## 6. FURTHER INFORMATION

In addition to the active ingredient, the medicine also contains:

Mannitol, Sodium citrate, Water for injection

What the medicine looks like and the contents of the package:

Zomera is supplied as a liquid concentrate in a vial. One vial contains 4 mg zoledronic acid.

Each pack contains 1, 4 or 10 vials. Not all pack sizes may be marketed.

**Registration holder and address:** Novartis Israel Ltd., 36 Shacham St., Petach-Tikva.

**Manufacturer and address:** Novartis Pharma Stein AG, Stein, Switzerland for Novartis Pharma AG, Basel, Switzerland.

This leaflet was checked and approved by the Ministry of Health in November 2016.

Registration number of the medicine in the National Drug Registry of the Ministry of Health:
129 53 30791

**INFORMATION FOR THE HEALTHCARE PROFESSIONAL**

**How to prepare and administer Zomera**

- To prepare an infusion solution containing 4 mg zoledronic acid, further dilute the Zomera concentrate (5.0 ml) with 100 ml of calcium-free or other divalent cation-free infusion solution. If a lower dose of Zomera 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 Zomera concentrate with calcium-containing or other divalent cation-containing solutions such as lactated Ringer's solution.**
  Instructions for preparing reduced doses of Zomera:
  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.
- After aseptic addition of Zomera 4 mg/5 ml concentrate for solution for infusion to the infusion media (sodium chloride 0.9% w/v or glucose 5% w/v), the Zomera solution for infusion should be used immediately. If the solution is not used immediately, storage prior to use is responsibility of the user and should be at 2°C – 8°C. The refrigerated solution should then be equilibrated to room temperature prior to administration. The cumulated time between dilution with infusion media, storage in a refrigerator and end of administration must not be longer than 24 hours.
- 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 Zomera to ensure that they are adequately hydrated.
- Studies with several types of infusion lines made from polyvinylchloride, polyethylene and polypropylene showed no incompatibility with Zomera.
- Since no data are available on the compatibility of Zomera with other intravenously administered substances, Zomera must not be mixed with other medications/substances and should always be given through a separate infusion line.

**How to store Zomera**

- Keep Zomera out of the reach and sight of children.
- Do not use Zomera after the expiry date stated on the pack.
- Do not store the unopened vial above 30°C.
- The diluted Zomera infusion solution should be used immediately in order to avoid microbial contamination.

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