**Package leaflet: Information for the user**

**Zoledronic acid Mylan 4 mg/100 ml 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. See section 4.

**What is in this leaflet**


## 1. What Zoledronic acid Mylan is and what it is used for

The active substance in Zoledronic acid Mylan 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 Mylan

Follow carefully all instructions given to you by your doctor.
Your doctor will carry out blood tests before you start treatment with Zoledronic acid Mylan and will check your response to treatment at regular intervals.

**You must not be given Zoledronic acid Mylan:**
− if you are breast-feeding.
− if you are allergic to zoledronic acid, another bisphosphonate (the group of substances to which Zoledronic acid Mylan belongs), or any of the other ingredients of this medicine (listed in section 6).

**Warnings and precautions**
Talk to your doctor, pharmacist or nurse before you are given Zoledronic acid Mylan:
− 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.
− if you are having **dental treatment** or are due to undergo dental surgery, tell your dentist that you are being treated with zoledronic acid and inform your doctor about your dental treatment.

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

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

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.

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 (see section 4 'Possible side effects').

Reduced levels of calcium in the blood (hypocalcaemia), sometimes leading to muscle cramps, dry skin, burning sensation, have been reported in patients treated with zoledronic acid. Irregular heart beat (cardiac arrhythmia), seizures (fits), numbness and twitching (tetany) have been reported as a result of severe hypocalcaemia. In some instances the hypocalcaemia may be life-threatening. If any of these apply to you, tell your doctor straight away. If you have pre-existing hypocalcaemia, it must be corrected before starting the first dose of zoledronic acid. You will be given adequate calcium and vitamin D supplements.

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

**Other medicines and Zoledronic acid Mylan**
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 taking:

- Aminoglycosides (medicines used to treat severe infections), calcitonin (a medicine used to treat post-menopausal osteoporosis and hypercalcaemia), loop diuretics (medicine used to treat high blood pressure or swelling) 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.
- Other medicines that also contain zoledronic acid and which are 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 Mylan are unknown.
- Anti-angiogenic medicines (used to treat cancer), since the combination of these with zoledronic acid has been associated with an increased risk of osteonecrosis of the jaw .

**Pregnancy and breast-feeding**
You should not be given Zoledronic acid Mylan if you are pregnant. Tell your doctor if you are or think that you may be pregnant.

You must not be given Zoledronic acid Mylan if you are breast-feeding.

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking any medicine

**Driving and using machines**
There have been cases of dizziness and sleepiness with the use of zoledronic acid. You should therefore be careful when driving, using machinery or performing other tasks that need full attention.

**Zoledronic acid Mylan contains sodium**
This medicinal product contains less than 1 mmol sodium (23 mg) per dose (100ml), i.e. essentially 'sodium-free'.

## 3. How Zoledronic acid Mylan is used

- Zoledronic acid Mylan 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 Zoledronic acid Mylan is given**

- The recommended dose given is 4 mg.
- If you have a kidney problem, your doctor may give you a lower dose depending on the severity of your kidney problem.

**How often Zoledronic acid Mylan 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 Mylan 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 Mylan.

**How Zoledronic acid Mylan is given**

- Zoledronic acid Mylan 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 who have low blood calcium levels will also be prescribed calcium and vitamin D supplements to be taken each day.

**If you are given more Zoledronic acid Mylan 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, this medicine can cause side effects, although not everybody gets them.

**Tell your doctor immediately or if serious, go to your nearest hospital emergency department if you get any of the following side effects:**

**Common (may affect up to 1 in 10 people):**

- Low levels of calcium in the blood which can be seen in a blood test. This may lead to muscle cramps or a tingling sensation especially around the mouth.

**Uncommon (may affect up to 1 in 100 people):**

- Producing little or no urine, pain when passing urine, urine is cloudy or dark coloured possibly with lower back pain. These may be signs of severe kidney problems.
- 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).

- A very fast and irregular heart rhythm (atrial fibrillation). This 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 reactions such as a red itchy skin rash (known as nettle rash or hives), a feeling of light headedness with possible collapse and unconsciousness.
- Low blood pressure leading to fainting or circulatory shock. You may be confused, have changes in your heart beat, clammy skin, thirst or a low body temperature.

**Rare (may affect up to 1 in 1,000 people):**
- Other problems with your heart beat (cardiac arrhythmia) which can be seen in an ECG. This may be as a result of low levels of calcium.
- Swelling of the face, lips, mouth, tongue or throat causing difficulty breathing or swallowing.
- A kidney function disorder called Fanconi syndrome (will normally be determined by your doctor with certain urine tests).

**Very rare (may affect up to 1 in 10,000 people):**
- Seizures (fits), numbness and twitching. These may be as a result of low levels of calcium.
- Talk to 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.
- Osteonecrosis has also very rarely been seen occurring with other bones than the jaw, especially the hip or thigh. Tell your doctor immediately if you experience symptoms such as new onset or worsening of aches, pain or stiffness while being treated with <Product name> or after stopping treatment.

**Other possible side effects:**

**Very common (may affect more than 1 in 10 people):**
- Low levels of phosphate in the blood which can be seen in a blood test.

**Common (may affect up to 1 in 10 people):**
- Headache
- Fever
- A flu-like syndrome consisting of headache, fever, tiredness, weakness, drowsiness, generally feeling unwell, flushing, chills, pain in the hands or feet, feeling sick (nausea), being sick (vomiting) and/or diarrhoea. In most cases no specific treatment is required and the symptoms disappear after a short time (couple of hours or days).
- Feeling sick (nausea), being sick (vomiting), decrease in appetite.
- Bone pain, muscle or joint ache, general pain.
- Swollen, runny eyes or a feeling of grit in the eyes (conjunctivitis).
- Tiredness, shortness of breath, looking pale. These may be signs of low level of red blood cells (anaemia).
- Other kidney problems that affect urination
- Creatinine and urea levels in the blood increased which can be seen in a blood test.

**Uncommon (may affect up to 1 in 100 people):**

- Other allergic reactions
- An increase in the number of infections causing fever, severe chills, mouth ulcers or sore throat. These may be signs of low levels of white blood cells.
- Redness or visible blood vessels on the whites of the eye, severe eye pain, pain in the eyebrow, temple or jaw, watery eyes, sensitivity to light.
- High blood pressure or low blood pressure.
- Chest pain.
- Skin reactions (pain, irritation, swelling or a hard lump) at the infusion site, rash, itching.
- Dizziness, anxiety, sleep disturbances, taste disturbances, trembling, tingling or numbness of the hands or feet, decrease or increase in sensitivity touch.
- Diarrhoea, constipation, stomach pain, indigestion, mouth ulcers or cold sores, dry mouth.
- Unexplained bruising or bleeding for longer than normal. These may be signs of low levels of blood platelets.
- Low levels of magnesium or potassium in the blood which can be seen in a blood test. Your doctor will monitor this and take any necessary measures.
- Weight increase.
- Increased sweating.
- Sleepiness.
- Blurred vision.
- Tightness of the chest with wheezing or coughing.
- Cough.
- Lack of energy.
- Swelling of the hands, ankles or feet.
- Muscle spasms.
- Blood in your urine.
- Protein in the urine which can be seen in a urine test.

**Rare (may affect up to 1 in 1,000 people):**

- Tiredness, weakness, being short of breath, looking pale with unexplained bruising or bleeding for longer than normal and signs of low levels of white blood cells (see description in 'Uncommon' above). These may be signs of low levels of all types of blood cells.
- Red eye with blurred or cloudy vision, shadows, dots or veils that move across the field of vision (floaters) in one or both eyes.
- Shortness of breath that gets worse over time with a dry and non-productive cough possibly with loss of weight. These may be signs of problems with your lungs.
- 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.
- Slow heartbeat.
- Confusion.
- High levels of potassium or sodium in the blood which can be seen in a blood test.

- Disease of the joints (arthritis) and joint swelling which may only last for a few days.

**Very rare (may affect up to 1 in 10,000 people):**
- Mild ache or soreness of the eyes.

**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 national reporting system:

HPRA
Pharmacovigilance
Earlsfort Terrace
IRL – Dublin 2
Tel: +353 1 6764971
Fax: +353 1 6762517
Website: www.hpra.ie
e-mail: medsafety@hpra.ie

By reporting side effects you can help provide more information on the safety of this medicine.

## 5. How to store Zoledronic acid Mylan

Your doctor, pharmacist or nurse knows how to store Zoledronic acid Mylan properly (see section 6).

## 6. Contents of the pack and other information

**What Zoledronic acid Mylan contains**
- The active substance is zoledronic acid. One vial contains 4 mg zoledronic acid, corresponding to 4.26 mg zoledronic acid monohydrate.
- The other ingredients are: mannitol (E421), sodium citrate (E331) (see section 'Zoledronic acid Mylan contains sodium'), water for injections.

**What Zoledronic acid Mylan looks like and contents of the pack**
Zoledronic acid Mylan is a clear, colourless solution, free from visible particles.
Zoledronic acid Mylan is supplied as a solution in a vial. One vial contains 4 mg of zoledronic acid.

Zoledronic acid Mylan is supplied as packs containing 1, 4 or 5 vials.

Not all pack sizes may be marketed.

**Marketing Authorisation Holder**
Generics [UK] Ltd., Potters Bar, Hertfordshire, EN6 1TL, United Kingdom

**Manufacturer**
Agila Specialties Polska Sp. Zo.o., 10, Daniszewska Str., 03-230 Warsaw, Poland
Sanochemia Pharmazeutica AG, Landeggerstrasse 7, A - 2491 Neufeld an der Leitha, Austria

**This medicinal product is authorised in the Member States of the EEA under the following names:**

| | |
|---|---|
| FRANCE | Acide Zolédronique Mylan Pharma 4 mg/100 ml solution pour perfusion |
| GERMANY | Zoledronsäure Mylan 4 mg/100ml Infusionslösung |
| IRELAND | Zoledronic acid Mylan 4 mg/100 ml solution for infusion |
| NETHERLANDS | Zoledroninezuur Mylan 4 mg/100 ml, oplossing voor infusie |
| POLAND | Zoledronic Acid Mylan |
| PORTUGAL | Ácido Zoledrónico Mylan |
| SLOVAKIA | Zoledronic acid Mylan 4 mg/100 ml, infúzny roztok |
| SLOVENIA | Zoledronska kislina Mylan 4 mg/100 ml raztopina za infundiranje |
| UNITED KINGDOM | Zoledronic acid Mylan 4 mg/100 ml, solution for infusion |

**This leaflet was last revised in August 2017.**

Detailed information on this medicine is available on the website of HPRA (www.hpra.ie).

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**The following information is intended for healthcare professionals only:**

**How to prepare and administer Zoledronic acid Mylan**

- 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.
- If refrigerated, allow the refrigerated solution to reach room temperature before administration.
- It is given as a single 15-minute intravenous infusion. Since no data are available on the compatibility of zoledronic acid with other intravenously administered substances, Zoledronic acid must not be mixed with other medications/substances and should always be given through a separate infusion line. The hydration status of patients must be assessed prior to and following administration of Zoledronic acid Mylan to ensure that they are adequately hydrated.
- Zoledronic acid Mylan can be used immediately without further preparation for patients with normal renal function. In patients with mild to moderate renal impairment, reduced doses should be prepared as instructed below.

To prepare reduced doses for patients with baseline CLcr ≤ 60 ml/min, refer to Table 1 below.

Remove the volume of Zoledronic acid Mylan solution indicated from the vial and replace with an equal volume of sterile sodium chloride 9 mg/ml (0.9%) solution for injection, or 5% glucose solution for injection.

**Table 1**: Preparation of reduced doses of Zoledronic acid Mylan

| Baseline creatinine clearance (ml/min) | Remove the following amount of Zoledronic acid Mylan (ml) | Replace with the following volume of sterile sodium chloride 9 mg/ml (0.9%) or 5% glucose solution for injection (ml) | Adjusted dose (mg zoledronic acid in 100 ml) |
|---|---|---|---|
| 50-60 | 12.0 | 12.0 | 3.5 |
| 40-49 | 18.0 | 18.0 | 3.3 |
| 30-39 | 25.0 | 25.0 | 3.0 |

*Doses have been calculated assuming target AUC of 0.66 (mg•hr/l) (CLcr = 75 ml/min). The reduced doses for patients with renal impairment are expected to achieve the same AUC as that seen in patients with creatinine clearance of 75 ml/min.

- Studies with several types of infusion lines made from polyvinylchloride, polyethylene and polypropylene showed no incompatibility with zoledronic acid.

**How to store Zoledronic acid Mylan**

- Keep this medicine out of the sight and reach of children.
- Do not use Zoledronic acid Mylan after the expiry date stated on the pack. The expiry date refers to the last day of that month.
- This medicinal product does not require any special storage conditions.

- After first opening or after preparation of reduced zoledronic acid doses (as described above): chemical and physical stability has been demonstrated for 24 hours at 2°C - 8°C and at 25°C. From a microbiological point of view, the 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.
- Do not throw away any medicines via wastewater. These measures will help protect the environment.