ZOLDRO
(Zoledronic Acid for Injection 4mg/Vial)

PATIENT INFORMATION LEAFLET

(For All Products not subject to Medical Prescription)

ZOLDRO (Zoledronic Acid for Injection 4mg/Vial)

PACKAGE LEAFLET: INFORMATION FOR THE USER

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 you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet.

In this leaflet:

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

The active substance in Zoledronic Acid Accord 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 Zoledronic Acid is given to you

Follow carefully all instructions given to you by your doctor.

Your doctor will carry out blood tests before you start treatment with Zoledronic Acid Accord and will check your response to treatment at regular intervals.

Do not receive Zoledronic Acid Accord:

If you are breast-feeding.

If you are allergic to zoledronic acid, another bisphosphonate (the group of substances to which Zoledronic Acid Accord belongs), or any of the other ingredients of this medicine.

Warnings and precautions

Talk to your doctor, pharmacist or nurse before you are given Zoledronic Acid Accord

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 Accord.

If you are having **dental treatment** or are due to undergo dental surgery, tell your dentist that you are being treated with Zoledronic Acid Accord and inform your doctor about your dental treatment.

While being treated with Zoledronic Acid Accord, 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.

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 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 Zoledronic Acid Accord. 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. If you have pre-existing hypocalcaemia, it must be corrected before initiating the first dose of Zoledronic Acid Accord. You will be given adequate calcium and vitamin D supplements.

Patients aged 65 years and over

Zoledronic Acid Accord 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 Accord is not recommended for use in adolescents and children below the age of 18 years.

Other medicines and Zoledronic Acid Accord

Tell your doctor or pharmacist 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.

Other medicines that also contain zoledronic acid and 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 Accord 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 (ONJ).

Pregnancy and breast-feeding

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

You must not be given Zoledronic Acid Accord if you are breast-feeding.

Ask your doctor for advice before taking any medicine 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 Accord.

You should therefore be careful when driving, using machinery or performing other tasks that need full attention.

Zoledronic Acid Accord contains sodium.

This medicinal product contains less than 1m mol sodium (23 mg) per vial, i.e. essentially 'sodium-free'.

3. How Zoledronic Acid is given to you

Zoledronic Acid Accord 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 Accord is given:

The usual single dose given is 4 mg zoledronic acid.

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 Accord 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 Accord 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 Accord.

How Zoledronic Acid Accord is given

Zoledronic Acid Accord 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 Accord 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.

If you have any further questions on the use of this medicine, ask your doctor, pharmacist or nurse.

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.

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 determined 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 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 Accord or after stopping treatment.

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.

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

As a consequence of low calcium values: 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 (may affect up to 1 in 10,000 people):

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

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 Zoledronic Acid Accord or after stopping treatment.

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, 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 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.

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

- Slow heartbeat.
- 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 Yellow Card Scheme Website:www.mhra.gov.uk/yellowcard. By reporting side affects you can help provide more information on the safety of this medicine.

5. How to store Zoledronic Acid

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

6. Contents of the pack and other information

What Zoledronic Acid Accord contains

The active substance is zoledronic acid. One vial contains 4 mg zoledronic acid (as monohydrate).

The other ingredients are: mannitol, sodium citrate, water for injections.

What Zoledronic Acid Accord looks like and contents of the pack

Zoledronic Acid Accord is supplied as a liquid concentrate in a vial. One vial contains 4 mg of zoledronic acid.

Each pack contains the vial with concentrate. Zoledronic Acid Accord is supplied as packs containing 1, 4 or 10 vials.

Not all pack sizes may be marketed.

Marketing Authorization Holder and Manufacturer

Name	**: Aspiro Pharma Limited**
Business Address	: Survey No.321, Biotech Park, Phase III, Karkapatla, Markook Mandal, Siddipet District, Telangana (S)- 5002281, INDIA.
Country	: INDIA
Telephone	: +91 9959644022, 9959644077

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