PART III: CONSUMER INFORMATION

[Pr]Zoledronic Acid for Injection

4 mg/5 mL (0.8 mg/mL)

zoledronic acid (as zoledronic acid monohydrate)

For Intravenous Infusion

This leaflet is part III of a three-part "Product Monograph" published when Zoledronic Acid for Injection was approved for sale in Canada and is designed specifically for Consumers. This leaflet is a summary and will not tell you everything about Zoledronic Acid for Injection. Contact your doctor or pharmacist if you have any questions about the drug.

Please read this information carefully before starting treatment with Zoledronic Acid for Injection.

ABOUT THIS MEDICATION

What the medication is used for:

Zoledronic Acid for Injection is used to:

1) reduce the abnormal amount of calcium in the blood for example, in the presence of a tumour. This is because 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.
2) prevent or delay skeletal complications for example, fractures of the bone and bone pain requiring surgery or radiotherapy, as a result of bone metastases (cancer that has spread from the tumour to the bone) due to different types of tumours.

What it does:

Zoledronic Acid for Injection is a member of a group of substances called bisphosphonates. These strongly bind to the bone and slow down the rate of bone change. In addition, Zoledronic Acid for Injection may prevent bone destruction and uncontrolled bone growth associated with the tumour spreading to the bone.

When it should not be used:

You should not be given Zoledronic Acid for Injection if you are:

- pregnant
- breastfeeding
- allergic to zoledronic acid, other bisphosphonates (the group of substances to which Zoledronic Acid for Injection belongs) or to any other nonmedicinal ingredients in Zoledronic Acid for Injection.
- hypocalcaemic (have low calcium levels in your blood)

What the medicinal ingredient is:

Zoledronic acid.

What the important nonmedicinal ingredients are:

Mannitol, sodium citrate dihydrate, and water for injection.

What dosage forms it comes in:

Zoledronic Acid for Injection is available in vials.

Each vial delivers 4 mg of zoledronic acid. They are available in cartons containing 1 vial.

WARNINGS AND PRECAUTIONS

Serious Warnings and Precautions

Serious side effects which have been reported with the use of Zoledronic Acid for Injection include:

- **osteonecrosis of the jaw (a severe bone disease that affects the jaw)**
- **deterioration in renal function.** Zoledronic Acid for Injection is not recommended in patients with severe kidney impairment.
- **hypocalcaemia** (low calcium levels in your blood)

If you are being treated with Zoledronic Acid for Injection, you should not be treated with another intravenous form of zoledronic acid or other bisphosphonates (e.g. alendronate, risedronate, clodronate, etidronate and pamidronate) at the same time.

Your doctor may request an oral examination (an examination of your mouth and teeth) before you start treatment and while you are on treatment with Zoledronic Acid for Injection. This may be required since some patients have experienced serious side effects following dental procedures (such as tooth extraction) while on Zoledronic Acid for Injection; as well, since patients with unhealed open wounds in the mouth, dental infections or periodontal disease (disease affecting the surrounding tissues of a tooth) may be at increased risk of problems with their jaw bones following dental procedures (such as tooth extraction) while on treatment with Zoledronic Acid for Injection.

You should avoid invasive dental procedures during your treatment with Zoledronic Acid for Injection. It is important that you practice good dental hygiene, routine dental care, and have regular dental check-ups while being treated with Zoledronic Acid for Injection. Immediately report any oral symptoms (any symptoms in your mouth), such as loosening of a tooth, pain, swelling, or non-healing of sores or discharge (pus or oozing) during your treatment with Zoledronic Acid for Injection.

BEFORE you use Zoledronic Acid for Injection, talk to your doctor or pharmacist if you:

- Have a kidney problem. Worsening of kidney function, including kidney failure (very rarely with fatal outcome), has been reported with the use of zoledronic acid.
- Have asthma and are also allergic to acetylsalicylic acid (ASA).

- Had or have a heart problem. Cases of irregular heart beat (atrial fibrillation) have been observed with the use of zoledronic acid.
- Have any dental problems or any dental procedures planned in the future.
- Have pain, swelling or numbness of the jaw, a "heavy jaw feeling", loosening of a tooth, or any other symptoms in your mouth.
- Have sores in your mouth. This can lead to osteonecrosis of the jaw. Your doctor may check if you:
    - smoke
    - have or have had tooth and/or gum disease
    - have dentures that do not fit well
    - have other medical conditions at the same time, such as: low red blood cell count (anaemia) or if your blood cannot form clots in the normal way.

Your doctor may tell you to stop taking Zoledronic Acid for Injection until all sores in your mouth are healed.

After starting treatment with Zoledronic Acid for Injection

It is important that your doctor checks your progress at regular intervals. He or she may want to take repeated blood tests, especially after starting your treatment with Zoledronic Acid for Injection.

If possible, you should not undergo tooth extraction or any other dental procedures (excluding regular dental cleaning) while you are receiving treatment with Zoledronic Acid for Injection. Please consult your doctor if a dental procedure (excluding regular dental cleaning) is required while you are receiving treatment with Zoledronic Acid for Injection. It is important to maintain good dental hygiene; regularly scheduled dental examinations are recommended.

Tell your doctor if you had or have joint stiffness, aches and pains and difficulty in movement of your thighs, hips, upper arms (in the bones between your shoulders and elbows), lower legs (in the long large bones between your knees and your feet), ribs, backbone, knees, or feet bones (in the five long bones between your ankles and your toes), or pain around your ears. Tell your doctor, as this may be a sign of bone damage due to loss of blood supply to the bone (osteonecrosis).

Driving and using machines

Zoledronic Acid for Injection may affect your ability to drive a car or to operate machinery. Do not drive a car or operate machinery until you know how Zoledronic Acid for Injection affects you.

Use in Children

Zoledronic Acid for Injection should not be used in children.

INTERACTIONS WITH THIS MEDICATION

Tell your doctor about any other medicines you are taking or have recently been taking, including any you have bought without a prescription. It is particularly important that your doctor knows if you are also taking aminoglycosides (a type of medicine used to treat severe infections), calcitonin (a type of medicine used to treat high calcium levels in the blood and Paget's disease), loop diuretics (a type of medicine used 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. Examples of aminoglycosides include gentamycin sulfate, tobramycin sulfate and streptomycin sulphate; examples of loop diuretics include furosemide, torsemide and ethacrinic acid.

It is also important to inform your doctor if you are taking any drugs that can have an effect on the kidney, since combining these drugs with Zoledronic Acid for Injection may cause kidney function to deteriorate. Some examples of these drugs include aminoglycosides, acetylsalicylic acid (ASA), nonsteroidal anti-inflammatories (e.g. ibuprofen, diclofenac, celecoxib), diuretics (e,g, hydrochlorothiazide, amiloride, spironolactone and indapamide), and Angiotensin-Converting Enzyme (ACE) inhibitors (e.g. enalapril, ramipril, fosinopril).

Tell your doctor if you are taking anti-angiogenic medicines (type of medicines used to treat cancer, e.g. thalidomide, bortezomid, lenalidomide, bevacizumab) as part of your cancer treatment because the combination of these medicines with bisphosphonates may increase the risk of bone damage in the jaw (osteonecrosis).

PROPER USE OF THIS MEDICATION

Usual dose:

Zoledronic Acid for Injection is given by an infusion into a vein which should last no less than 15 minutes. The dose is usually 4 mg. If you have a kidney problem, your doctor may give you a lower dose depending on the severity of your kidney problem.

If you are being treated for multiple myeloma or bone metastases of solid tumours, you will be given one infusion of Zoledronic Acid for Injection every three to four weeks. If you require antineoplastic therapy (therapy that blocks the growth of cancer cells), Zoledronic Acid for Injection should be administered either prior to, or after this treatment. You will also be asked to take an oral calcium supplement of 500 mg and a multivitamin containing at least 400 IU of Vitamin D daily. If you have a prior history of high levels of calcium in the blood or develop high levels of calcium in the blood during treatment with calcium and Vitamin D, you may be advised to discontinue taking calcium and Vitamin D supplements by your doctor.

Your doctor will decide how many infusions you need and how often you should receive them.

If you are being treated for Tumour-Induced Hypercalcaemia (TIH), you will normally only be given one infusion of Zoledronic Acid for Injection. Prior to treatment with Zoledronic Acid for Injection, restoring and maintaining adequate fluid regulation in your body and urine output may help to eliminate excess calcium from your kidneys.

Overdose:

In case of drug overdose, contact a health care practitioner, hospital emergency department or regional Poison Control Centre immediately, even if there are no symptoms. You may develop serum electrolyte abnormalities and changes in kidney function, including severe kidney impairment.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

Like all medicines, Zoledronic Acid for Injection may have, in addition to its beneficial effects, some unwanted effects. These are usually mild and will probably disappear after a short time. The most common side effect is short-lasting fever. Patients may experience a flu-like condition including fever, fatigue, weakness, drowsiness and chills. In some patients, these symptoms may also be accompanied by bone, joint and/or muscle ache, arthritis and joint swelling. In most cases, no specific treatment is required and the symptoms subside after a couple of hours or days. Other common side effects include gastrointestinal problems such as nausea, vomiting and thirst as well as swelling of sores inside the mouth and loss of appetite.

Occasionally, skin reactions (redness and swelling) at the infusion site may occur. Cases of low blood pressure have also occasionally been reported; in very rare cases, this resulted in fainting.

Rare cases of rash, itching, chest pain, swelling mainly of the face and throat, high level of potassium and sodium in the blood, slow heart beat, confusion, and a disorder of the kidney function called Fanconi syndrome have been observed.

Very rare cases of severe bone, joint, and/or muscle pain, occasionally incapacitating, as well as sleepiness, irregular heart beat (atrial fibrillation), difficulty breathing with wheezing or coughing, lung disease, severe allergic reaction and itchy rash have also been reported.

Reduced levels of calcium in the blood (hypocalcaemia), sometimes leading to muscle cramps, dry skin or burning sensation, have been reported in patients treated with zoledronic acid. Irregular heart beat has also been reported. There have been reports of abnormal electrical signals of the heart called "prolongation of the QT interval", seizures, numbness, spasm and twitching caused by severely reduced levels of calcium in the blood. In some instances, the reduced calcium level may be life-threatening and require hospitalization. If any of these apply to you, **tell your doctor right away**.

Blood tests indicating worsening of kidney function (higher levels of creatinine) including severe kidney failure have been reported with Zoledronic Acid for Injection; such changes are also known to occur with other drugs of the bisphosphonate class. Your doctor will carry out blood tests to monitor your kidney function prior to each dose of Zoledronic Acid for Injection. If these tests indicate worsening of kidney function, your doctor will withhold further treatment with Zoledronic Acid for Injection until these tests have returned to normal.

The level of calcium, phosphate and/or magnesium in the blood may become too low, but your doctor will monitor this and take necessary measures.

Other bisphosphonates can cause breathing difficulties in patients with asthma who are allergic to acetylsalicylic acid (ASA). This has not been reported with Zoledronic Acid for Injection, in studies done to date.

Eye pain, redness, photophobia (sensitivity to light), excessive tearing or decreased vision should be reported to your physician as they may indicate more serious eye complications which have been associated with Zoledronic Acid for Injection.

Some patients have reported problems with their jaw bones while receiving cancer treatments that include Zoledronic Acid for Injection. Dental hygiene is an important element of your overall cancer care and is important in possibly decreasing the chances of this type of problem occurring. Removable dentures should fit properly and should be removed at night. Please consult with your doctor if you experience pain in your mouth, teeth or jaw, or if your gums or mouth heals poorly. Any non-healing of a dental extraction site or chronic dental infection should be reported and assessed. In addition, if possible you should not undergo tooth extraction or other dental procedures (excluding regular dental cleaning) while on therapy with Zoledronic Acid for Injection. Please consult your doctor if a dental procedure (excluding regular dental cleaning) is required while you are receiving treatment with Zoledronic Acid for Injection.

Some patients have reported problems with other bones, other than their jaw bones, while on treatment with Zoledronic Acid for Injection. Consult your doctor if you had or have aches and pains and difficulty in movement of your thighs, hips, upper arms, lower legs, ribs, backbone, knees, or feet bones, or if you experience pain around your ears.

Unusual fracture of the thigh bone may occur while receiving treatment with Zoledronic Acid for Injection. Contact your doctor if you experience pain, weakness or discomfort in your thigh, hip or groin as this may be an early sign of a possible fracture of the thigh bone.

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM

Symptom / effect		Talk with your doctor or pharmacist		Stop taking drug and call your doctor or pharmacist
		Only if severe	In all cases	
Common	• Worsening of kidney function (higher levels of creatinine)			√
	• Bone, joint and/or muscle pain, joint stiffness	√		

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM				
Symptom / effect		**Talk with your doctor or pharmacist**		**Stop taking drug and call your doctor or pharmacist**
		Only if severe	**In all cases**	
	• Conjunctivitis		√	
Uncommon	• Kidney failure (changes in urine colour or absence of urine production, changes in kidney function laboratory tests, lower back pain, fatigue, nausea, loss of appetite)			√
	• Eye disorders (painful red and/or swollen eye, excessive tearing, light sensitivity, or decreased vision)		√	
	• Allergic reaction to zoledronic acid (swelling of the face, eyes or tongue, difficulty breathing, hives, rash, sudden onset of low blood pressure)			√
	• Dizziness			√
	• Osteonecrosis of the jaw (numbness or feeling of heaviness in the jaw, poor healing of the gums especially after dental work, loose teeth, exposed bone in mouth, pain in the mouth, teeth or jaw, sores or non-healing sores in the mouth or discharge (pus or oozing), swelling, dry mouth, swelling gum infections, or bad breath.			√
	• Osteonecrosis of other bones (joint stiffness, aches and pains, and difficulty in movement of the thighs, hips, upper arms, lower legs, ribs, backbone, knees, or feet bones, or pain around the ears)			√
Unknown[1]	• Difficulty breathing with wheezing or coughing			√
	• Irregular heart beat (atrial fibrillation)			√
	• Sleepiness	√		
	• Severe allergic reaction			√
	• Itchy rash			√
	• Thigh pain, weakness or discomfort/ Unusual fracture of the thigh bone			√
	• Muscle cramps or twitching, dry skin, burning sensation, or irregular heartbeat		√	
	• Disorder in kidney function with release of amino acids, phosphate and glucose in urine (acquired Fanconi syndrome)			√

[1] The frequency with which these side effects may occur cannot be reliably estimated.

This is not a complete list of side effects. If you have any unexpected effects after receiving Zoledronic Acid for Injection, contact your doctor or pharmacist.

HOW TO STORE IT

Zoledronic Acid for Injection:
Store at room temperature (between 15°C - 30°C).

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Zoledronic Acid for Injection must be kept out of reach and sight of children and pets.

Reporting Suspected Side Effects

You can report any suspected adverse reactions associated with the use of health products to the Canada Vigilance Program by one of the following 3 ways:

- Report online at https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/adverse-reaction-reporting.html
- Call toll-free at 1-866-234-2345
- Complete a Canada Vigilance Reporting Form and:
  - Fax toll-free to 1-866-678-6789, or
  - Mail to: Canada Vigilance Program
    Health Canada
    Postal Locator 1908C
    Ottawa, ON K1A 0K9

  Postage paid labels, Canada Vigilance Reporting Form and the adverse reaction reporting guidelines are available on the MedEffect™ Canada Web site athttps://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/adverse-reaction-reporting.html.

NOTE: Should you require information related to the management of side effects, contact your health professional. The Canada Vigilance Program does not provide medical advice.

MORE INFORMATION

This document plus the full product monograph, prepared for health professionals can be found by contacting the sponsor, Pfizer Canada Inc., at: **1-800-463-6001**.

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