

PART III: CONSUMER INFORMATION

PrZOMETA® Concentrate
(Zoledronic acid for Injection)
For Intravenous Infusion

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

Please read this information carefully before starting treatment with ZOMETA (zoledronic acid for injection).

ABOUT THIS MEDICATION**What the medication is used for:**

ZOMETA 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:

ZOMETA 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, ZOMETA 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 ZOMETA if you are:

- pregnant
- breastfeeding
- allergic to zoledronic acid, other bisphosphonates (the group of substances to which ZOMETA belongs) or to any other non medicinal ingredients in ZOMETA
- hypocalcaemic (have low calcium levels in your blood)

What the medicinal ingredient is:

Zoledronic acid.

What the important nonmedicinal ingredients are:

Mannitol and sodium citrate.

What dosage forms it comes in:

ZOMETA is available as a concentrate in vials. Each vial of

ZOMETA concentrate delivers 4 mg of zoledronic acid. It is available in cartons containing 1 vial.

WARNINGS AND PRECAUTIONS**Serious Warnings and Precautions**

Serious side effects which have been reported with the use of ZOMETA include:

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

If you are being treated with ZOMETA, you should not be treated with another intravenous form of zoledronic acid (i.e. ACLASTA®) 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 ZOMETA. This may be required since some patients have experienced serious side effects following dental procedures (such as tooth extraction) while on ZOMETA; 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 ZOMETA.

You should avoid invasive dental procedures during your treatment with ZOMETA. It is important that you practice good dental hygiene, routine dental care, and have regular dental check-ups while being treated with ZOMETA. 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 ZOMETA.

BEFORE you use ZOMETA 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 ZOMETA.
- 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 ZOMETA.
- 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 ZOMETA until all sores in your mouth are healed.

After starting treatment with ZOMETA

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 ZOMETA.

If possible, you should not undergo tooth extraction or any other dental procedures (excluding regular dental cleaning) while you are receiving treatment with ZOMETA. Please consult your doctor if a dental procedure (excluding regular dental cleaning) is required while you are receiving treatment with ZOMETA. 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

ZOMETA may affect your ability to drive a car or to operate machinery. Do not drive a car or operate machinery until you know how ZOMETA affects you.

Use in Children

ZOMETA 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 ZOMETA 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:

ZOMETA 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 ZOMETA every three to four weeks. If you require antineoplastic therapy (therapy that blocks the growth of cancer cells), ZOMETA 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 ZOMETA. Prior to treatment with ZOMETA, 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, ZOMETA 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 ZOMETA. 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 ZOMETA; 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 ZOMETA. If these tests indicate worsening of kidney function, your doctor will withhold further treatment with ZOMETA 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 ZOMETA, 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 ZOMETA.

Some patients have reported problems with their jaw bones while

receiving cancer treatments that include ZOMETA. 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 ZOMETA. Please consult your doctor if a dental procedure (excluding regular dental cleaning) is required while you are receiving treatment with ZOMETA.

Some patients have reported problems with other bones, other than their jaw bones, while on treatment with ZOMETA. 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 ZOMETA. 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	<ul style="list-style-type: none"> Worsening of kidney function (higher levels of creatinine) Bone, joint and/or muscle pain, joint stiffness Conjunctivitis 	√	√	√

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Symptom / effect		Talk with your doctor or pharmacist		Stop taking drug and call your doctor or pharmacist
		Only if severe	In all cases	
Uncommon	<ul style="list-style-type: none"> • 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 ZOMETA (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) 		√	√

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	
Unknown¹	<ul style="list-style-type: none"> • 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 heart beat • Disorder in kidney function with release of amino acids, phosphate and glucose in urine (acquired Fanconi syndrome) 	√	√	√

¹The 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 ZOMETA, contact your doctor or pharmacist.

HOW TO STORE ZOMETA

Vials (concentrate)

- Store ZOMETA vials at room temperature (between 15°C - 30°C).

ZOMETA 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 www.healthcanada.gc.ca/medeffect
- 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 0701E
 Ottawa, ON K1A

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Postage paid labels, Canada Vigilance Reporting Form and the adverse reaction reporting guidelines are available on the MedEffect™ Canada Web site at www.healthcanada.gc.ca/medeffect.

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 at:

www.novartis.ca

Or by contacting the sponsor:

Novartis Pharmaceuticals Canada Inc. at: 1-800-363-8883

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