

**Regimen Monograph**

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**A - Regimen Name**

# ZOLE Regimen

Zoledronic Acid

**Disease Site**      Genitourinary  
                                 Prostate

**Intent**              Palliative

**Regimen Category**      **Evidence-Informed :**

Regimen is considered appropriate as part of the standard care of patients; meaningfully improves outcomes (survival, quality of life), tolerability or costs compared to alternatives (recommended by the Disease Site Team and national consensus body e.g. pan-Canadian Oncology Drug Review, pCODR). Recommendation is based on an appropriately conducted phase III clinical trial relevant to the Canadian context OR (where phase III trials are not feasible) an appropriately sized phase II trial. Regimens where one or more drugs are not approved by Health Canada for any indication will be identified under Rationale and Use.

**Rationale and Uses**      For the treatment of bone metastases in patients with hormone refractory prostate cancer

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**B - Drug Regimen**[zoledronic acid](#)

4 mg

IV

Day 1

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All patients, especially those with hypercalcemia, should be adequately hydrated. Calcium and Vitamin D supplements should be considered in patients who have normal calcium levels with no history of hypercalcemia. (Refer to zoledronic acid monograph).

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Doses should be modified according to the protocol by which the patient is being treated. The following recommendations have been adapted from clinical trials or product monographs and could be considered. Hypocalcemia must be corrected before administering zoledronic acid.

Do not administer to patients with open soft tissue lesions in the mouth.

**Dosage with toxicity**

Dosage in myelosuppression: No dosage adjustment required

Toxicity	Action
Atypical fractures of the femur	Hold if suspected. Consider discontinuing if confirmed.
Ocular symptoms other than uncomplicated conjunctivitis	Refer to ophthalmologist; consider discontinuing
Osteonecrosis of the jaw, other sites	For ONJ, refer to dentist or dental surgeon; consider hold or discontinue
Severe musculoskeletal pain	Discontinue
Acquired Fanconi syndrome	Discontinue
Increased creatinine: 1. $\geq 44 \mu\text{mol/L}$ $\uparrow$ if normal baseline** OR 2. $\geq 88 \mu\text{mol/L}$ $\uparrow$ if abnormal at baseline OR 3. Serum creatinine $> 265 \mu\text{mol/L}$ ( $> 400 \mu\text{mol/L}$ with TIH)	Hold until recovered to within 10% of baseline (see table for dose adjustment for renal impairment at baseline)

\*\*normal baseline creatinine is defined as  $< 123 \mu\text{mol/L}$

### **Hepatic Impairment**

There are no pharmacokinetic (PK) data in patients with impaired liver function. Zoledronic acid is not cleared by the liver; therefore, impaired liver function may not affect the PK of zoledronic acid.

### **Renal Impairment**

			Starting Dose
Creatinine		Creatinine Clearance (mL/min)	For bone metastases
		$> 60$	4 mg
		50 - 60	3.5 mg
		40 - 49	3.3 mg
		30 - 39	3 mg
$> 265 \mu\text{mol/L}$ ( $> 400 \mu\text{mol/L}$ with TIH)	Or	$< 30$	Do not treat

**Dosage in the Elderly**

Similar efficacy and safety as compared to younger patients, but use with caution due to cardiac risks or renal function impairment.

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**F - Adverse Effects**

Refer to [zoledronic acid](#) drug monograph(s) for additional details of adverse effects

Common (25-49%)	Less common (10-24%)	Uncommon (< 10%), but may be severe or life-threatening
<ul style="list-style-type: none"> <li>• Nausea, vomiting</li> <li>• Fatigue, flu-like symptoms</li> <li>• Cough, dyspnea (may be severe)</li> </ul>	<ul style="list-style-type: none"> <li>• Diarrhea</li> <li>• Musculoskeletal pain (may be severe)</li> <li>• Edema</li> <li>• Headache</li> <li>• Dizziness</li> <li>• Nephrotoxicity (may be severe)</li> <li>• Weight loss</li> <li>• Paresthesia</li> <li>• Depression</li> <li>• Abnormal electrolytes</li> <li>• Conjunctivitis</li> </ul>	<ul style="list-style-type: none"> <li>• Atypical fractures of the femur</li> <li>• Atrial fibrillation, arrhythmia</li> <li>• Osteonecrosis of the jaw (ONJ) or other sites</li> <li>• Hypersensitivity</li> <li>• Eye disorders</li> <li>• Acquired Fanconi syndrome</li> </ul>

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**G - Interactions**

Refer to [zoledronic acid](#) drug monograph(s) for additional details

- Caution and monitor with drugs that cause hypocalcemia (e.g. aminoglycosides, loop diuretics, calcitonin)

- Caution and monitor with drugs that cause renal dysfunction (e.g. NSAIDs, ACE inhibitors)
- Avoid in patients with hypersensitivity to ASA given possible increased risk of bronchospasm (theoretical)
- Caution with antiangiogenic drugs (e.g. sunitinib, bevacizumab) given increased risk of ONJ

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## H - Drug Administration and Special Precautions

Refer to [zoledronic acid](#) drug monograph(s) for additional details

### Administration:

- Do not infuse over a duration of less than 15 minutes.
- All patients should be adequately hydrated prior to and after administration of zoledronic acid, but overhydration should be avoided.
- Mix with 100 mL solution (D5W or NS) and infuse over  $\geq 15$  minutes.
- Do not mix with calcium or other divalent cation-containing solutions.
- Compatible with PVC, glass, polyethylene and polypropylene containers or infusion lines.
- Should be administered as a single intravenous solution in a line separate from all other drugs.
- Store unopened vials at room temperature.

### Contraindications:

- Patients who have a hypersensitivity to this drug or any of its components, or other bisphosphonates
- Patients with non-corrected hypocalcemia at time of infusion or severe renal failure
- Zoledronic acid should not be given together with other bisphosphonates since the combined effects of these agents are unknown

### Other Warnings/Precautions:

- The use of zoledronic acid with other nephrotoxins, doses  $> 4$ mg, infusion duration  $< 15$  minutes and previous bisphosphonate use are associated with an increased risk of renal failure.
- Use with caution in patients with cardiac failure, especially in the elderly.
- Use with caution in patients with risk factors for ONJ, including patients receiving concomitant chemotherapy or anti-angiogenic agents; patients should be advised to avoid invasive dental procedures while receiving zoledronic acid.
- Caution in patients who have had thyroid surgery since they are susceptible to hypocalcaemia due to relative hypoparathyroidism.

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## I - Recommended Clinical Monitoring

Treating physicians may decide to monitor more or less frequently for individual patients but should always consider recommendations from the product monograph.

### Recommended Clinical Monitoring

- Renal function tests (serum creatinine and BUN); baseline, before each dose and during therapy, as indicated
- Calcium, corrected levels (including serum albumin), electrolytes (including phosphate, magnesium); baseline, before each dose and during therapy, as indicated
- CBC; baseline and as clinically indicated
- Comprehensive dental evaluation of both hard and soft tissues before starting bisphosphonate treatment; undergo invasive dental procedures, if needed, before starting bisphosphonate treatment; regular check-ups
- Clinical toxicity assessment for flu-like syndrome, dental, signs of acquired Fanconi syndrome, musculoskeletal and ocular symptoms; at each visit
- Grade toxicity using the current [NCI-CTCAE \(Common Terminology Criteria for Adverse Events\) version](#)

### Suggested Clinical Monitoring

- Ophthalmology examination with ocular symptoms; as clinically indicated

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## J - Administrative Information

Approximate Patient Visit	0.5 hour
Pharmacy Workload (average time per visit)	16 minutes
Nursing Workload (average time per visit)	35 minutes

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## K - References

Himelstein AL et al. J Clin Oncol 2015;33 (suppl; abstr 9501).

Saad F, Gleason DM, Murray R et al. A randomized, placebo-controlled trial of zoledronic acid in

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patients with Hormone-refractory metastatic prostate carcinoma. JNCI 2002; 94(19): 1458-68.

Zoledronic acid drug monograph, Cancer Care Ontario.

### **PEBC Advice Documents or Guidelines**

- [Bone Health and Bone-Targeted Therapies for Prostate Cancer](#)

**April 2023** removed NDFP form

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## **M - Disclaimer**

### **Regimen Abstracts**

*A Regimen Abstract is an abbreviated version of a Regimen Monograph and contains only top level information on usage, dosing, schedule, cycle length and special notes (if available). It is intended for healthcare providers and is to be used for informational purposes only. It is not intended to constitute or be a substitute for medical advice, and all uses of the Regimen Abstract are subject to clinical judgment. Such information is provided on an “as-is” basis, without any representation, warranty, or condition, whether express, or implied, statutory or otherwise, as to the information’s quality, accuracy, currency, completeness, or reliability, and Cancer Care Ontario disclaims all liability for the use of this information, and for any claims, actions, demands or suits that arise from such use.*

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### **Regimen Monographs**

*Refer to the [New Drug Funding Program](#) or [Ontario Public Drug Programs](#) websites for the most up-to-date public funding information.*

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*Some Formulary documents, such as the medication information sheets, regimen information sheets and symptom*

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