**Regimen Monograph**



## A - Regimen Name

# DENO Regimen

**Denosumab**

**Disease Site**

Breast
Genitourinary
- Renal Cell / Kidney

Lung
- Mesothelioma (Pleural)
- Non-Small Cell
- Small Cell
- Thymoma

Unknown Primary

**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 reducing the risk of developing skeletal-related events in patients with bone metastases.

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## B - Drug Regimen

Different denosumab products are **not interchangeable**.

| | | | |
|---|---|---|---|
| **denosumab** | 120 mg | Subcut | Day 1 |

**(This drug is not currently publicly funded for this regimen and intent)**

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## C - Cycle Frequency

**REPEAT EVERY 28 DAYS**

Unless unacceptable toxicity

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## D - Premedication and Supportive Measures

**Antiemetic Regimen:** Not applicable

**Other Supportive Care:**

All patients, except those with hypercalcemia, should receive the following supplementation:

- at least 500mg of calcium daily
- at least 400 IU of vitamin D daily

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## E - Dose Modifications

Doses should be modified according to the protocol by which the patient is being treated.

Pre-existing hypocalcemia must be corrected prior to starting treatment.

Patients being treated with denosumab should not be treated concomitantly with bisphosphonates or other denosumab products.

### Dosage with toxicity

| Toxicity | Action |
|---|---|
| Grade 3 or 4 drug-related toxicity | Consider holding or discontinuing |
| Osteonecrosis of the jaw | Follow guidelines for management. Consider holding or discontinuing treatment. Refer patient to dentist or oral surgeon. |
| Hypocalcemia | Treat appropriately. Consider holding or discontinuing treatment if severe. |
| Anaphylaxis or significant hypersensitivity | Treat appropriately. Discontinue denosumab permanently. |

### Hepatic Impairment

No studies have been conducted in patients with hepatic impairment.

### Renal Impairment

No dose adjustment is required with renal impairment. Patients with renal impairment are at increased risk of severe life threatening hypocalcemia and require increased monitoring (refer to monitoring section).

### Dosage in the Elderly

No adjustment required. No overall differences in safety and efficacy.

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## F - Adverse Effects

Refer to denosumab drug monograph(s) for additional details of adverse effects.

| Common (25-49%) | Less common (10-24%) | Uncommon (< 10%),<br><br>but may be severe or life-threatening |
|---|---|---|
| • Nausea and vomiting<br>• Fatigue<br>• Anemia<br>• Musculoskeletal pain | • Anorexia, weight loss<br>• Constipation<br>• Diarrhea<br>• Abdominal pain<br>• Cough, dyspnea (may be severe)<br>• ↓ PO4, ↓ Ca (may be severe)<br>• Headache<br>• Fever | • Arterial thromboembolism<br>• Venous thromboembolism<br>• Renal failure<br>• Arrhythmia, cardiotoxicity<br>• Bone fracture (including atypical femoral; multiple vertebral after treatment discontinuation)<br>• Osteonecrosis of the jaw<br>• ↑ LFTs (may be severe)<br>• Cellulitis<br>• Hypersensitivity |

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## G - Interactions

Refer to denosumab drug monograph(s) for additional details.

- Exercise caution when given with drugs that may cause hypocalcemia. Monitor calcium levels closely.

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## H - Drug Administration and Special Precautions

Refer to denosumab drug monograph(s) for additional details.

Different denosumab products are **not interchangeable**.

### Administration:

- Inject subcutaneously in the upper arm, upper thigh, or the abdomen.
- Should not be administered intravenously, intramuscularly or intradermally
- Use a 27-gauge needle to withdraw or inject the drug. Avoid vigorous shaking of the drug.
- Denosumab should appear clear, colourless to slightly yellow. It may contain trace amounts of translucent or white proteinaceous particles. Do not use if the solution is discoloured, cloudy, contains many particles or foreign matter.
- If a dose is missed, it may be given as soon as possible and the subsequent injection should be scheduled q4 weeks from the most recent injection date.
- Keep refrigerated in the original carton between 2-8°C. Protect from direct light
- Before use, the drug vial (in its original container) can be brought to room temperature (usually takes 15-30 minutes). Do not warm the drug by other methods. Once removed from the refrigerator, it must be stored at room temperature (≤ 25°C) and used within 30 days.

### Contraindications:

- Contraindicated in patients who have a hypersensitivity to this drug or any of its components
- Hypocalcemia

### Precautions:

- Patients being treated with denosumab should not be treated concomitantly with bisphosphonates or other denosumab products.
- Risk of hypocalcemia is greater in patients with moderate to severe renal impairment. Patients, except those with hypercalcemia, should receive adequate calcium and vitamin D supplementation (see Dosing section).
- A risk-benefit assessment should be performed for patients with risk factors for ONJ before starting treatment.
- Dental examination with appropriate preventative dentistry should be considered prior to treatment. Invasive dental surgeries should be avoided while on treatment.

**Pregnancy/Lactation:**

- This regimen is not recommended for use in pregnancy. Adequate contraception should be used by patients and their partners while on treatment and after the last treatment dose. Recommended methods and duration of contraception may differ depending on the treatment. Refer to the drug monograph(s) for more information.
- Breastfeeding is not recommended during treatment and after the last treatment dose. Refer to the drug monograph(s) for recommendations after the last treatment dose (if available).
- Fertility effects: Unlikely

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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

- Calcium, phosphate, magnesium - No hypercalcemia: baseline, within 2 weeks of the first dose, and as clinically indicated. In patients with hypercalcemia: baseline, before each dose and as clinically indicated. Additional monitoring with renal dysfunction, symptoms of hypercalcemia / hypocalcemia, and after denosumab discontinuation in patients with growing skeletons
- Oral / dental examination; Baseline and regular
- Clinical toxicity assessment for fatigue, musculoskeletal effects, hypocalcemia, ONJ, hypersensitivity, cellulitis, cough/dyspnea; At each visit
- Vertebral fractures; evaluate patient risk after treatment discontinuation
- Grade toxicity using the current NCI-CTCAE (Common Terminology Criteria for Adverse Events) version

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## J - Administrative Information

| | |
|---|---|
| Approximate Patient Visit | 15 minutes |
| Pharmacy Workload (average time per visit) | 13.85 minutes |
| Nursing Workload (average time per visit) | 25.833 minutes |

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## K - References

Denosumab drug monograph, Ontario Health (Cancer Care Ontario).

Henry DH, Costa L, Goldwasser F, et al. Randomized, double-blind study of denosumab versus zoledronic acid in the treatment of bone metastases in patients with advanced cancer (excluding breast and prostate cancer) or multiple myeloma. J Clin Oncol 2011;29(9):1125-32.

Stopeck AT, Lipton A, Body JJ, et al. Denosumab Compared With Zoledronic Acid for the Treatment of Bone Metastases in Patients With Advanced Breast Cancer: A Randomized, Double-Blind Study. J Clin Oncol 2010;28(35):5132-9.

Vadhan-Raj S, von Moos R, Fallowfield LJ, et al. Clinical benefit in patients with metastatic bone disease: results of a phase 3 study of denosumab versus zoledronic acid. Ann Oncol 2012;23:3045-51.

**PEBC Advice Documents or Guidelines**

- Role of Bone-Modifying Agents in Metastatic Breast Cancer: An ASCO-CCO Focused Guideline Update

**August 2024** Added statement on biosimilar products; updated Adverse Effects, Contraindications, Precautions, Pregnancy/lactation, and Monitoring sections

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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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