Regimen Monograph

A - Regimen Name

PMDR(HYPER CA) Regimen

Pamidronate

Disease Site	Breast Central Nervous System Endocrine Gastrointestinal Genitourinary Gynecologic Head and Neck Hematologic Lung Sarcoma Skin Unknown Primary
Intent	Supportive Care 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	Treatment of tumour-induced hypercalcemia, following adequate saline rehydration

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B - Drug Regimen

pamidronate	90 mg	IV	Day 1

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C - Cycle Frequency

Single dose. Allow a minimum of 7 days prior to retreatment.

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D - Premedication and Supportive Measures

Other Supportive Care:

- All patients should be adequately hydrated.

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E - Dose Modifications

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

Dosage with toxicity

Dosage in myelosuppression: No dosage adjustment required.

Non-hematologic Toxicity	Action
Osteonecrosis of jaw	Refer patient to dentist or dental surgeon; consider hold or discontinue.
Atypical fractures of the femur	Consider discontinuing
Severe musculoskeletal pain	Discontinue
Ocular symptoms other than uncomplicated conjunctivitis	Refer to ophthalmologist; consider discontinuing.
Nephrotoxicity	Hold until recovered to within 10% of baseline (see table below for renal impairment at baseline).

Hepatic Impairment

AUC is increased in mild to moderate hepatic impairment but not considered clinically relevant; no dosage adjustment is required. No data available in patients with severe hepatic dysfunction and so should be used with caution.

Renal Impairment

Patients with severe renal impairment (< 30 mL/min) have 3 times higher pamidronate exposure than those with normal renal function.

Baseline	
Renal impairment	**Action**
CrCl > 90 mL/min	No adjustment needed
CrCl 30-90 mL/min	Do not exceed infusion rate of 22.5 mg/h
CrCl < 30 mL/min or Serum creatinine > 440 µmol/L (tumour induced hypercalcemia)	Only use for life-threatening hypercalcemia where the benefit exceeds risk

Dosage in the Elderly

No data available.

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F - Adverse Effects

Refer to pamidronate 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
• Flu-like symptoms	• Headache • Musculoskeletal pain (may be severe) • Cough, dyspnea • Anorexia • Abnormal electrolytes • Abdominal pain • Dyspepsia	• Arrhythmia, atrial fibrillation • Cardiotoxicity (due to fluid overload) • Hypersensitivity • Myelosuppression • Atypical fractures • Osteonecrosis (jaw, external ear canal) • Nephrotoxicity • Increased LFTs • Pneumonitis • Ocular (conjunctivitis, uveitis) • Viral reactivation • Seizure

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G - Interactions

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

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H - Drug Administration and Special Precautions

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

Administration

- Pamidronate must **not** be mixed with calcium-containing solutions (e.g., Ringer's solution).
- Pamidronate is generally mixed in 250-500mL solution (D5W or NS) and infused IV over 2-4 hours.
- According to the product monograph, it is recommended not to exceed 90 mg in 500 mL over 4 hours (i.e. 22.5 mg/h infusion rate) in multiple myeloma and tumour-induced hypercalcemia.
- Pamidronate must never be given as a bolus injection because of the risk of thrombophlebitis, severe local reactions and renal failure; it should always be diluted and administered as a slow IV infusion.
- All patients, especially those who are dehydrated or hypercalcemic, must be adequately rehydrated prior to treatment with pamidronate.
- Store unopened vials at room temperature (15-25°C). Protect vials from heat.

Contraindications:

- Patients with known or suspected hypersensitivity to pamidronate, or any of its components, or to other bisphosphonates
- Pregnant and/or breastfeeding women

Warnings/Precautions:

- Pamidronate should not be given together with other bisphosphonates to treat hypercalcemia, since the combined effects of these agents are unknown.
- Patients must be adequately hydrated throughout treatment, but special care should be taken in the elderly and patients with cardiac disease, to prevent fluid overload and cardiac failure.
- Avoid in patients with severe renal impairment, except in life-threatening cases of hypercalcemia.
- Use with caution in patients with risk factors for ONJ (see adverse effects description section).
- Patients should not drive, operate machinery or perform tasks that require alertness if they experience somnolence and/or dizziness after infusion.

Pregnancy/Lactation:

- Pamidronate is **contraindicated** in pregnancy. Adequate contraception should be used by both sexes during treatment, and for at least **6 months** after the last dose (general recommendation).
- Breastfeeding is **contraindicated**.
- Fertility effects: Probable

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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

- Dental examination with appropriate preventative dentistry should be considered prior to treatment. Regular dental check- ups. Avoid invasive dental surgeries while on treatment.
- Renal function tests; Baseline and at each visit
- Electrolytes, including corrected serum calcium, phosphates, magnesium, and serum albumin; Baseline and as clinically indicated
- Fluid balance (e.g. urine output, daily weights), especially in patients with pre-existing renal disease or risk of renal impairment; As clinically indicated
- Clinical toxicity assessment (including flu-like syndrome, hypersensitivity, hydration status, pain, dental, otic and ocular effects); At each visit

- Grade toxicity using the current NCI-CTCAE (Common Terminology Criteria for Adverse Events) version

Suggested Clinical Monitoring

- CBC, in patients with anemia, leukopenia, or thrombocytopenia; Baseline and as clinically indicated

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J - Administrative Information

Approximate Patient Visit	4 hours
Pharmacy Workload (average time per visit)	17.3 minutes
Nursing Workload (average time per visit)	45 minutes

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K - References

Nussbaum SR, Younger J, Vandepol CJ, et al. Single-dose intravenous therapy with pamidronate for the treatment of hypercalcemia of malignancy: comparison of 30-, 60-, and 90-mg dosages. Am J Med 1993;95(3):297.

Purohit OP, Radstone CR, Anthony C, Kanis JA, Coleman RE. A randomised double-blind comparison of intravenous pamidronate and clodronate in the hypercalcaemia of malignancy. Br J Cancer. 1995 Nov;72(5):1289-93.

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

January 2024 Dosage in renal impairment and Administration 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.

Information in regimen abstracts is accurate to the extent of the ST-QBP regimen master listings, and has not undergone the full review process of a regimen monograph. Full regimen monographs will be published for each ST-QBP regimen as they are developed.

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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