Regimen Monograph

A - Regimen Name

DEXAPOMA Regimen

Dexamethasone-Pomalidomide

Disease Site

Hematologic
Multiple Myeloma

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 relapsed or refractory multiple myeloma (MM) in:

- Patients who have progressed on lenalidomide;
- AND have previously failed OR may have a contraindication OR demonstrated an intolerance to bortezomib;
- AND have demonstrated disease progression following the last treatment used for MM

Supplementary Public Funding	**pomalidomide** Exceptional Access Program (pomalidomide - For patients with relapsed and/or refractory multiple myeloma, according to specific criteria.) (EAP Website) **dexamethasone** ODB - General Benefit (dexamethasone)

back to top

B - Drug Regimen

pomalidomide	4 mg	PO daily	Days 1 to 21

Pomalidomide may only be prescribed and dispensed by physicians and pharmacists registered with a controlled distribution program. Patients must also be registered and meet all conditions of the program.

dexamethasone	40* mg	PO	Days 1, 8, 15 and 22

*Decrease dexamethasone dose to 20 mg in patients > 75 years old

back to top

C - Cycle Frequency

REPEAT EVERY 28 DAYS

Until disease progression or unacceptable toxicity

back to top

D - Premedication and Supportive Measures

Antiemetic Regimen: Minimal – No routine prophylaxis; PRN recommended

- Also refer to CCO Antiemetic Recommendations.

Screen for hepatitis B virus in all cancer patients starting systemic treatment. Refer to the hepatitis B virus screening and management guideline.

Other Supportive Care:

- Prophylactic antithrombotics, such as low dose aspirin, low molecular weight heparins or warfarin, are recommended.
- Patients at risk of tumour lysis syndrome should have appropriate prophylaxis and be monitored closely.

back to top

E - Dose Modifications

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

Women of child bearing potential must have two negative pregnancy tests before initiating treatment.

Start treatment only if ANC ≥ 1 x 10^9/L and platelets ≥ 50 x 10^9/L.

Dosage with toxicity

Dexamethasone doses may be held or reduced for dexamethasone-related adverse events (i.e. hypertension, hyperglycemia, fluid retention) to improve tolerability.

Pomalidomide:

Dose Level	Pomalidomide Dose (mg/day)
0	4
-1	3
-2	2
-3	1
-4	Discontinue

Toxicity			Dose of Pomalidomide*
ANC (10^9/L) < 0.5 or Febrile neutropenia (fever ≥ 38.5^{0}C and ANC < 1)	or	Platelets (10^9/L) < 25	Hold, monitor CBC weekly, consider G-CSF. Restart* after recovery with 1 dose level ↓.
Grade 2 or 3 skin rash			Hold or discontinue. Resume if benefit outweighs potential risk.
Grade 4 rash or rash with exfoliation, bullae or purpura, angioedema, anaphylaxis, or suspected SJS/TEN/DRESS			Discontinue.
Grade 3 or 4 non-hematologic/organ toxicities			Hold until recovery* then ↓ 1 dose level. Consider discontinuing if grade 4.
Acute onset or worsening of pulmonary symptoms			Hold and investigate for pneumonitis. Resume only after an evaluation of the benefits and risks.
PML			Hold and investigate. Discontinue if confirmed.

*Do not re-start until ANC returns to ≥ 1 x 10^9/L and platelets ≥ 50 x 10^9/L, and non-hematological toxicities resolve to ≤ grade 2.

Hepatic Impairment

Pomalidomide is primarily metabolized in the liver. Hepatic impairment results in a 51-72% increase in drug exposure.

The starting dose should be adjusted as follows:

Hepatic Impairment*	Pomalidomide Starting Dose (mg/day)
Child-Pugh class A or B	3
Child-Pugh class C	2

*Product monograph states that use should be avoided in patients with serum bilirubin > 1.5 x ULN and AST/ALT > 3 x ULN.

Renal Impairment

Pomalidomide and its metabolites are renally excreted. Pomalidomide is dialysable.

The starting dose should be adjusted for severe impairment requiring dialysis, as follows:

Creatinine Clearance (mL/min)	Pomalidomide Starting Dose (mg/day)
< 30 requiring dialysis	3 (taken after dialysis)

Dosage in the Elderly

No dose adjustment for pomalidomide is required based on age. No overall differences in effectiveness were observed.

Patients > 65 years were observed to have higher incidences of infection and pneumonia than younger patients; dexamethasone holds or reductions may be required.

There is limited information in patients over 75 years old.

back to top

F - Adverse Effects

Refer to pomalidomide, dexamethasone 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
• Myelosuppression +/- infection (including atypical, viral reactivation), bleeding (may be severe) • Fatigue	• Constipation • Diarrhea • Cough, dyspnea (may be severe) • Musculoskeletal pain • Edema • Nausea, vomiting • Peripheral neuropathy • Anorexia	• Cardiotoxicity • Atrial fibrillation • Venous thromboembolism • Hypersensitivity • SJS/ TEN • DRESS • Renal failure • Tumour lysis syndrome • Secondary malignancy (non-melanoma skin cancer) • Increased LFTs • Pneumonitis • PML

back to top

G - Interactions

Refer to pomalidomide, dexamethasone drug monograph(s) for additional details.

- Avoid strong inhibitors of CYP1A2 if possible. If not possible to avoid, reduce the pomalidomide dose by 50%.
- Avoid CYP1A2 inducers if possible; cigarette smoking may reduce the efficacy of pomalidomide.
- Pomalidomide increases thromboembolic risk and would have an additive effect if co-administered with other thromboembolic agents. Hormonal contraceptives are not recommended due to the increased risk of thromboembolism.

back to top

H - Drug Administration and Special Precautions

Refer to pomalidomide, dexamethasone drug monograph(s) for additional details.

Administration

Pomalidomide may only be prescribed and dispensed by physicians and pharmacists registered with a controlled distribution program. Patients must also be registered and meet all conditions of the program.

- Capsule should be swallowed whole with a glass of water. Do not crush or open the capsule.
- Doses may be administered with or without food.
- Missed dose: If less than 12 hours has passed since the missed dose, the dose may be taken. If more than 12 hours has passed since the missed dose, skip this dose and take the next one at its usual time the next day. Do not give a double dose to make up for a missed one.
- On dialysis days, administer pomalidomide after the completion of hemodialysis due to possible significant decrease in drug exposure.
- Females who could become pregnant or who plan to become pregnant can handle pomalidomide capsules if they are using latex gloves.
- Store at room temperature (15-30°C) in original package in order to protect from light.

Contraindications

- Patients who have a hypersensitivity to this drug, any of its components, or to thalidomide or lenalidomide
- Patients who are pregnant, at risk of becoming pregnant, or are breastfeeding (Refer to Pregnancy and Lactation section)
- Male patients unable to comply with required contraceptive measures

Warnings/Precautions

- Avoid use in patients with active / history of hepatitis A, B, or C.
- Avoid use in patients taking other immunosuppressive treatments, to reduce the risk of developing serious infections.
- Patients should not donate blood or semen while taking pomalidomide, during treatment interruptions, and for 4 weeks after treatment cessation.
- Use with caution and consider prophylaxis when used in combination with corticosteroids or thrombogenic agents, such as hormones and erythropoietin or in patients with risk factors for arterial or venous thromboembolism (e.g. hypertension, hyperlipidemia, previous history of thromboembolism, or taking other agents that increase thromboembolic risk.
- Use with caution in patients with pre-existing ≥ grade 2 neuropathy.
- Use with caution when operating machinery, or when driving, as confusion, fatigue, depressed level of consciousness and dizziness may occur with treatment.

- Use with caution in patients with significant cardiac dysfunction (i.e. CHF NYHA Class III or IV, MI within 12 months, unstable or poorly controlled angina) as pomalidomide use has not been studied in these patients. Atrial fibrillation has occurred, especially in patients with pre-existing cardiac disease or cardiac risk factors.
- In clinical trials, increased mortality was observed when pembrolizumab was added to dexamethasone and a thalidomide analogue.

Pregnancy/Lactation

- Pomalidomide is **contraindicated in pregnancy and in males and females of childbearing potential who do not comply with the contraception conditions of the controlled distribution program**. Refer to the controlled distribution program for full details.
- Breastfeeding is contraindicated.
- Fertility effects:
  - Pomalidomide: Probable

back to top

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.

Refer to the hepatitis B virus screening and management guideline for monitoring during and after treatment.

Recommended Clinical Monitoring

- CBC; Baseline, weekly for the first 8 weeks then monthly thereafter
- Liver function tests; Baseline and at each visit
- Renal function tests; Baseline and at each visit
- Controlled distribution program requirements regarding pregnancy tests for women of child-bearing potential; Before starting, during treatment and for at least 4 weeks after discontinuation
- Clinical toxicity assessment for infection, bleeding, hypersensitivity, thromboembolism, secondary malignancies, pneumonitis, hepatitis, TLS, neurological and skin effects; At each visit
- Grade toxicity using the current NCI-CTCAE (Common Terminology Criteria for Adverse Events) version

back to top

J - Administrative Information

Outpatient prescription for home administration

back to top

K - References

Pomalidomide drug monograph. Ontario Health (Cancer Care Ontario).

San Miguel J et al. Pomalidomide plus low-dose dexamethasone versus high-dose dexamethasone alone for patients with relapsed and refractory multiple myeloma (MM- 003): a randomized, open-label, phase 3 trial. Lancet Oncol 2013;14:1055-66.

PEBC Advice Documents or Guidelines

- Treatment of Multiple Myeloma: ASCO and CCO Joint Clinical Practice Guideline

April 2023 Updated adverse effects and dose modifications sections

back to top

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.

The information set out in the drug monographs, regimen monographs, appendices and symptom management information (for health professionals) contained in the Drug Formulary (the "Formulary") is intended for healthcare providers and is to be used for informational purposes only. The information is not intended to cover all possible uses, directions, precautions, drug interactions or adverse effects of a particular drug, nor should it be construed to indicate that use of a particular drug is safe, appropriate or effective for a given condition. The information in the Formulary is not intended to constitute or be a substitute for medical advice and should not be relied upon in any such regard. All uses of the Formulary are subject to clinical judgment and actual prescribing patterns may not follow the information provided in the Formulary.

The format and content of the drug monographs, regimen monographs, appendices and symptom management information contained in the Formulary will change as they are reviewed and revised on a periodic basis. The date of last revision will be visible on each page of the monograph and regimen. Since standards of usage are constantly evolving, it is advised that the Formulary not be used as the sole source of information. It is strongly recommended that original references or product monograph be consulted prior to using a chemotherapy regimen for the first time.

Some Formulary documents, such as the medication information sheets, regimen information sheets and symptom management information (for patients), are intended for patients. Patients should always consult with their healthcare provider if they have questions regarding any information set out in the Formulary documents.

While care has been taken in the preparation of the information contained in the Formulary, 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.

CCO and the Formulary’s content providers shall have no liability, whether direct, indirect, consequential, contingent, special, or incidental, related to or arising from the information in the Formulary or its use thereof, whether based on breach of contract or tort (including negligence), and even if advised of the possibility thereof. Anyone using the information in the Formulary does so at his or her own risk, and by using such information, agrees to indemnify CCO and its content providers from any and all liability, loss, damages, costs and expenses (including legal fees and expenses) arising from such person’s use of the information in the Formulary.

back to top