BC Cancer Protocol Summary for Therapy of Multiple Myeloma using Pomalidomide with Dexamethasone

Protocol Code	*UMYPOMDEX*
Tumour Group	*Myeloma*
Contact Physician	*Dr. Christopher Venner*

ELIGIBILITY:

Patients must have:

- Relapsed/refractory multiple myeloma,
- Previously received prior therapy that has included lenalidomide and a proteasome inhibitor (may have been discontinued due to progression or intolerance), and
- A BC Cancer "Compassionate Access Program" request with appropriate clinical information approved prior to treatment

Registration of the prescribing physician and patient with the RevAid Program (www.RevAid.ca) is required.

Note:

- Cyclophosphamide may be added per physician discretion to increase response

EXCLUSIONS:

Patients must not:

- Be pregnant or lactating
- Have a known hypersensitivity to pomalidomide

CAUTIONS:

- Platelet count less than 30×10^9/L
- ANC less than 1.0×10^9/L. Consider giving filgrastim
- Previous hypersensitivity to lenalidomide or thalidomide

TESTS:

- Baseline (required before first treatment): CBC & Diff, platelets, creatinine, urea, sodium, potassium, total bilirubin, ALT, alkaline phosphatase, calcium, albumin, LDH, random glucose. If female of child-bearing potential (FCBP): Confirm negative pregnancy test results via a quantitative beta-hCG blood test obtained 7 to 14 days and 24 hours prior to initial prescription.
- Baseline (required, but results do not have to be available to proceed with first treatment; results must be checked before proceeding with cycle 2): serum protein electrophoresis and serum free light chain levels, immunoglobulin panel (IgA, IgG, IgM), HCAb, HBsAg, HBcoreAb, TSH, beta-2 microglobulin
- Every 4 weeks (required, but results do not have to be available to proceed with treatment): serum protein electrophoresis and serum free light chain levels
- Every 4 weeks (optional, results not mandatory but encouraged prior to each cycle): urine protein electrophoresis, immunoglobulin panel (IgA, IgG, IgM), beta-2 microglobulin
- Every 4 weeks: CBC & Diff, platelets, creatinine, urea, sodium, potassium, total bilirubin, ALT, alkaline phosphatase, calcium, albumin, LDH, random glucose; if female of childbearing potential: quantitative beta-hCG blood test
- Days 8, 15, 22 (optional if pre-cycle cytopenias, hypercalcemia, hepatic or renal dysfunction, or steroid-induced diabetes a concern. Results do not have to be available to proceed with treatment. Provider to review results, no dose modifications indicated for mid-cycle bloodwork): CBC & Diff, platelets, creatinine, sodium, potassium, total bilirubin, ALT, alkaline phosphatase, calcium, albumin, random glucose
- Every three months (required, but results do not have to be available to proceed with treatment): TSH
- If female of childbearing potential: Every week for 4 weeks during cycle 1: quantitative beta-hCG blood test. Provider responsible for checking results.

PREMEDICATIONS:

None

SUPPORTIVE MEDICATIONS:

- If HBsAg or HBcoreAb positive, start hepatitis B prophylaxis as per current guidelines
- Antiviral prophylaxis against reactivation of varicella-zoster virus (VZV) is recommendedprior to initiating pomalidomide. Patients should take valACYclovir 500 mg PO daily
- Oral proton-pump inhibitor or H_2 antagonist for the duration of treatment with dexamethasone or prednisone may be considered
- ASA (enteric coated), warfarin, direct oral anticoagulant (DOAC) PO or low molecular weight heparin (LMWH) SC daily continuing for the duration of treatment with pomalidomide

TREATMENT:

Drug	Dose	BC Cancer Administration Guideline
dexamethasone	*40 mg once weekly on Days 1, 8, 15 and 22	PO, in the morning may be preferred
pomalidomide	4 mg once daily for 21 days (Days 1 to 21)	PO, in the evening may be preferred
OPTIONAL cyclophosphamide¥	500 mg once weekly on Days 1, 8, 15 and 22 *OR* 50 mg once every 2 days	PO, in the morning may be preferred

* Dexamethasone dose may vary dependent on tolerability and co-morbidities. For older patients i.e. 75 years of age or older, the starting dose of dexamethasone should be 20 mg PO weekly. See also: Other options for steroid dosing, below

¥ cyclophosphamide may be added per physician discretion to increase response.

Repeat every 28 until progression or unacceptable toxicity.

OTHER OPTIONS FOR STEROID DOSING

Option A: **dexamethasone 20 mg PO once weekly** (or dexamethasone 4 to 40 mg PO once weekly based on toxicity and patient tolerance)
Option B: predniSONE may be substituted for patient or physician preference, in a variety of regimens based upon toxicity and patient tolerance. (e.g. predniSONE 10 to 100 mg PO once weekly)
Option C: No dexamethasone/predniSONE. High-dose steroids may need to be avoided in certain patients who are intolerant or have difficulty with side-effects. It is expected that the response will be inferior than with high-dose steroids. High-dose steroids may be added for non-response.

POMALIDOMIDE DOSE MODIFICATIONS:
NB: Use one of the 1 mg, 2 mg, 3 mg or 4 mg capsules for dosing. Currently there is no evidence to support the use of other dosing regimens (i.e., there is no clinical reason or research available to support the use of a combination of pomalidomide capsules for dosing, however the use of such dosing does have significant budgetary implications).

Pomalidomide Dose Levels:

Dose Level 0	Dose Level -1	Dose Level -2	Dose Level -3
4 mg	3 mg	2 mg	1 mg

1. Hematological:(based on pre-cycle labwork):

ANC ($x\ 10^9$/L) on Day 1		Platelets ($x\ 10^9$/L) on Day 1	Pomalidomide Dose	Cyclophosphamide Dose (if using)
Greater than or equal to 1.0	and	Greater than or equal to 50	100%	100%
0.5 to 0.99†	or	30 to 49	Notify provider. Proceed but at next lower dose level, above.	Delay until recovery
less than 0.5 or febrile neutropenia (ANC less than 1.0 with oral temperature greater than or equal to 38.0° Celsius)	or	less than 30*	Hold pomalidomide until ANC greater than or equal to 1.0 and platelets greater than or equal to 30, then restart at next lower dose level, above.	

* follow hematology weekly and consider arrangements for transfusion support as required.

† Consider weekly filgrastim if clinically indicated and filgrastim is available. Filgrastim is not covered as a benefit drug by BC Cancer.

2. Hepatic Impairment:

Hepatic impairment	Pomalidomide Dose	Cyclophosphamide (if using)
Mild or moderate (Child-Pugh Class A or B)	3 mg	No adjustment required
Severe (Child-Pugh Class C)	2 mg	

Pomalidomide is metabolized in the liver

3. Renal Impairment: pomalidomide

Estimated GFR (eGFR) or Creatinine clearance (mL/min)	Pomalidomide Dose
Less than 30 including dialysis dependence	3 mg* *For patients on hemodialysis, on hemodialysis days, take pomalidomide following hemodialysis

Pomalidomide and its metabolites are excreted by the kidneys

Renal Impairment: cyclophosphamide

- Renal failure: dose reduction is necessary per table, below. Physician may consider giving full dose of cyclophosphamide irrespective of renal function if deemed to be of benefit.
- For patients on hemodialysis, give dose after dialysis.

Creatinine clearance (mL/min)	Cyclophosphamide Dose
Greater than or equal to 10	100 %
Less than 10	75 %

Calculated creatinine clearance = $\frac{N \times (140 - Age) \times weight\ (kg)}{Serum\ Creatinine\ (micromols/L)}$

N = 1.04 (Females) and 1.23 (Males)

PRECAUTIONS:

1. **Teratogenicity**: If pomalidomide is taken during pregnancy, it may cause severe birth defects or death to the fetus. Pomalidomide should never be used by females who are pregnant or who could become pregnant while taking the drug. Even a single dose taken by a pregnant woman may cause birth defects.
2. **Venous thrombosis/embolism:** Pomalidomide with dexamethasone is known to increase the risk for thromboembolic disease. **ASA 81 mg** oral daily should be considered in all patients. For those with higher risk of thrombo-embolic disease, full anti-coagulation should be considered.
3. **Hepatitis B Reactivation**: All myeloma patients should be tested for both HBsAg and HBcAb. If either test is positive, such patients should be treated with hepatitis B prophylaxis according to current guidelines. Such patients should also be monitored with frequent liver function tests and hepatitis B virus DNA at least every three months. If the hepatitis B virus DNA level rises during this monitoring, management should be reviewed with an appropriate specialist with experience managing hepatitis and consideration given to halting chemotherapy.
4. **Need for irradiated blood products:** Patients receiving an autotransplant require irradiated blood products from 7 days prior to collection to 3 months post transplant (6 months if total body irradiation conditioning) to eliminate the risk of potentially life-threatening transfusion-related graft-versus-host-disease. All other myeloma patients do not require irradiated blood products

Call Dr. Christopher Venner or tumour group delegate at 604-877-6000 or 1-800-663-3333 with any problems or questions regarding this treatment program.

References:

1. San Miguel J, Weisel K, Moreau P, 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(21):1055-66.
2. Richardson PG, Siegal DS, Vij R, et al. Pomalidomide alone or in combination with low-dose dexamethasone in relapsed and refractory multiple myeloma: a randomized phase 2 study. Blood 2014;123(12):1826-32.
3. Pomalidomide Product Monograph, April 7, 2017. Celgene Inc.