

# BCCA Protocol Summary for Therapy of Multiple Myeloma Using Lenalidomide with Dexamethasone

<b>Protocol Code</b>	<b>UMYLENDEX</b>
<b>Tumour Group</b>	<b>Lymphoma, Leukemia/BMT</b>
<b>Contact Physician</b>	<b>Dr. Kevin Song</b>
<b>Contact Pharmacist</b>	<b>Linda Hamata</b>

## ELIGIBILITY:

- For the treatment of multiple myeloma in patients who received at least one prior therapy
- A BC Cancer Agency “Compassionate Access Program” request with appropriate clinical information for each patient must be approved prior to treatment
- Registration of the prescribing physician and patient with the RevAid Program ([www.RevAid.ca](http://www.RevAid.ca))

## EXCLUSIONS:

- Pregnant or lactating women
- Platelet count less than  $30 \times 10^9 /L$  may be considered a relative contraindication.
- If absolute neutrophil count (ANC) less than  $1.0 \times 10^9 /L$  may be considered a relative contraindication. Consider giving filgrastim
- Known hypersensitivity to lenalidomide or thalidomide

## TESTS:

- Baseline (required before first treatment): CBC & diff, platelets, creatinine. If female of child-bearing potential: pregnancy test (blood) or evidence of hysterectomy
- Baseline (required, but results do not have to be available to proceed with first treatment): calcium and serum protein electrophoresis, HBsAg, HBcoreAb, TSH
- Every 2 weeks for the first 4 cycles then may reduce frequency to every 4 weeks: CBC and diff, platelets, creatinine, calcium
- Every 4 weeks (required before treatment): CBC and diff, platelets, creatinine; if female of childbearing potential: pregnancy test (blood)
- Every 4 weeks (required, but results do not have to be available to proceed with treatment): calcium and serum protein electrophoresis; **free light chain if clinically indicated**
- Every three months (required, but results do not have to be available to proceed with treatment): T3, T4, TSH

## PREMEDICATIONS:

None

## TREATMENT:

### Cycles 1-4

Drug	Dose	BCCA Administration Guideline
Lenalidomide	25 mg once daily for 21 days (d 1-21)	PO, in the evening may be preferred
Dexamethasone	40 mg once daily on days 1-4, 9-12, 17-20	PO, in the morning may be preferred

Repeat every 28 days for 4 cycles

### Cycles 5 and subsequent cycles

Drug	Dose	BCCA Administration Guideline
Lenalidomide	25 mg once daily for 21 days (d 1-21)	PO, in the evening may be preferred
Dexamethasone	40 mg once daily on days 1-4	PO, in the morning may be preferred

Repeat every 28 days until progression of the myeloma or unacceptable toxicity

## OTHER OPTIONS FOR DEXAMETHASONE DOSING

### Option A:

Oral dexamethasone 20mg daily on days 1-4, 9-12, 17-20 x 4 cycles; then 20 mg daily on days 1-4 only for subsequent cycles. The dose should be adjusted based upon toxicity and patient tolerance.

### Option B:

Oral dexamethasone 40mg weekly on days 1, 8, 15 and 22 for all cycles. The dose should be adjusted based upon toxicity and patient tolerance.

### Option C:

Prednisone may be substituted for patient or physician preference, in a variety of regimens based upon toxicity and patient tolerance.

### Option D:

No dexamethasone. Dexamethasone 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 using lenalidomide alone. Dexamethasone may be added for non-response.

Repeat every 28 days until progression of the myeloma or unacceptable toxicity

## LENALIDOMIDE DOSE MODIFICATIONS:

Fatigue may respond to dose reduction

NB: Use one of the 25 mg, 15 mg, 10 mg or 5 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 lenalidomide capsules for dosing, however the use of such dosing does have significant budgetary implications).

### 1. Hematological:

#### Neutropenia

Initial dose*	ANC (x10 <sup>9</sup> /L)	Dose*
25 mg	Day 1 of Cycle less than 1	Hold until ANC greater than or equal to 1†, then resume at 25 mg dose plus filgrastim 5 mcg/kg; if filgrastim not available <b>consider</b> resuming at 15 mg dosing (Filgrastim is not covered as a benefit at the BCCA)
	Day 15 of Cycle‡ less than 1	Omit for remainder of cycle; restart on Day 1 of next cycle if ANC greater than or equal to 1†; <b>consider</b> resuming at 15 mg dose
15 mg	Day 1 of Cycle less than 1	Hold until ANC greater than or equal to 1†, then restart; <b>consider</b> resuming at 10 mg dose
	Day 15 of Cycle‡ less than 1	Omit for remainder of cycle; restart on Day 1 of next cycle if ANC greater than or equal to 1†; <b>consider</b> resuming at 10 mg dose
10 mg	Day 1 of Cycle less than 1	Hold until ANC greater than or equal to 1†, then restart; <b>consider</b> resuming at 5 mg dose
	Day 15 of Cycle‡ less than 1	Omit for remainder of cycle; restart on Day 1 of next cycle if ANC greater than or equal to 1†; <b>consider</b> resuming at 5 mg dose
5 mg	Day 1 of Cycle less than 1	<b>Consider</b> stopping treatment, otherwise hold until ANC greater than or equal to 1†, then restart
	Day 15 of Cycle‡ less than 1	<b>Consider</b> stopping treatment, otherwise omit for remainder of cycle; restart on Day 1 of next cycle if ANC greater than or equal to 1†

\* dosing for 21 days (d 1-21) of each 28-day cycle

† follow hematology weekly

‡ Day 15 bloodwork for Cycle 1-4 will be monitored by the physician and physician will be responsible to check and advise patient on dose adjustment based on ANC

◆ may use filgrastim if clinically indicated and filgrastim is available.

## Thrombocytopenia

Initial dose*	Platelet (x10 <sup>9</sup> /L)	Dose*
25 mg	Day 1 of Cycle less than 30	Hold until platelet greater than or equal to 30†, and no evidence of hemostatic failure (i.e., bleeding or petechiae), then restart; <b>consider</b> resuming at 15 mg dose
	Day 15 of Cycle‡ less than 30	Omit for remainder of cycle; restart on Day 1 of next cycle if platelet greater than or equal to 30†; <b>consider</b> resuming at 15 mg dose
15 mg	Day 1 of Cycle less than 30	Hold until platelet greater than or equal to 30†, and no evidence of hemostatic failure (i.e., bleeding or petechiae), then restart; <b>consider</b> resuming at 10 mg dose
	Day 15 of Cycle‡ less than 30	Omit for remainder of cycle; restart on Day 1 of next cycle if platelet greater than or equal to 30†; <b>consider</b> resuming at 10 mg dose
10 mg	Day 1 of Cycle less than 30	Hold until platelet greater than or equal to 30†, and no evidence of hemostatic failure (i.e., bleeding or petechiae), then restart; <b>consider</b> resuming at 5 mg dose
	Day 15 of Cycle‡ less than 30	Omit for remainder of cycle; restart on Day 1 of next cycle if platelet greater than or equal to 30†, <b>consider</b> restarting at 5 mg dose
5 mg	Day 1 of Cycle less than 30	<b>Consider</b> stopping treatment; otherwise hold until platelet greater than or equal to 30†, and no evidence of hemostatic failure (i.e., bleeding or petechiae), then restart
	Day 15 of Cycle‡ less than 30	<b>Consider</b> stopping treatment; otherwise omit for remainder of cycle; restart on Day 1 of next cycle if platelet greater than or equal to 30†,

\* dosing for 21 days (d 1-21) of each 28-day cycle

† follow hematology weekly

‡ Day 15 bloodwork for Cycle 1-4 will be monitored by the physician and physician will be responsible to check and advise patient on dose adjustment based on platelets

## 2. Renal dysfunction:

Estimated GFR (eGFR)* or Creatinine clearance (mL/min)	Dose
greater than or equal to 60	25 mg†
30-59	10 mg†‡
less than 30, not requiring dialysis	15 mg every other day for 21 days, then rest for 7 days (i.e. 28-day cycle) <sup>4</sup>
less than 30, dialysis dependent	5 mg† (administer after dialysis)

\*as reported in patient's laboratory report

†dosing for 21 days (d 1-21) of each 28-day cycle

‡dose can be escalated to 15 mg after 2 cycles if patient is not responding to treatment and is tolerating the drug; **may consider escalating to 25 mg if patient continues to tolerate the drug.**

### PRECAUTIONS:

- 1. Teratogenicity:** If lenalidomide is taken during pregnancy, it may cause severe birth defects or death to the fetus. Lenalidomide 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. Constipation:** Patients should be warned that constipation may occur in patients taking lenalidomide.
- 3. Fatigue:** Patients should be warned that lenalidomide may cause fatigue.
- 4. Hypothyroidism:** the use of lenalidomide may result in hypothyroidism. Thyroid function tests should be repeated every 3 months. Treatment with thyroid replacement should be considered even for subclinical hypothyroidism. Lenalidomide can be continued if hypothyroidism can be easily managed.
- 5. Venous thrombosis/embolism:** Lenalidomide with dexamethasone is known to increase the risk for thromboembolic disease. **Aspirin 81mg** oral daily should be considered in all patients. For those with higher risk of thrombo-embolic disease full anti-coagulation should be considered.
- 6. Hepatitis B Reactivation:** All myeloma patients should be tested for both HBsAg and HBcoreAb. If either test is positive, such patients should be treated with Lamivudine 100 mg/day orally, for the entire duration of chemotherapy and for six months afterwards. Such patients should also be monitored with frequent liver function tests and hepatitis B virus DNA at least every two 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.
- 7. Skin Rashes:** Lenalidomide may cause skin rashes although in general it is not severe. Minor rashes can be treated with diphenhydramine and/or steroid creams

and lenalidomide can be continued. Moderate rashes may require holding lenalidomide until resolution of the rash. For more severe rashes (greater than or equal to Grade 3: severe, generalized erythroderma or macular, papular or vesicular eruption; desquamation covering greater than or equal to 50% BSA) lenalidomide should be discontinued.

**Call Dr. Kevin Song (Leukemia/BMT) or Dr Laurie Sehn (Lymphoma) or tumour group delegate with any problems or questions regarding this treatment program. (Leukemia/BMT at (604) 875-4863 or after hours (604) 875-4111; Lymphoma at (604) 877-6000 or 1-800-663-3333)**

**Date activated:** 1 Dec 2008

**Date revised:** 1 Jan 2012 (revised wording for hematological dose modifications, revised renal dose modifications and protocol contact information)

**References:**

1. Dimopoulos M, Spencer A, Attal M, et al. Multiple Myeloma (010) Study Investigators. Lenalidomide plus dexamethasone for relapsed or refractory multiple myeloma. *N Engl J Med* 2007;357:2123-32.
2. Weber DM, Chen C, Niesvizky R, et al. Multiple Myeloma (009) Study Investigators. Lenalidomide plus dexamethasone for relapsed multiple myeloma in North America. *N Engl J Med* 2007;357:2133-42.
3. Palumbo A, Rajkumar SV, Dimopoulos MA et al. Prevention of thalidomide- and lenalidomide-associated thrombosis in myeloma. *Leukemia* 2008;22:414-23.
4. Kevin Song MD, Personal communication. BC Cancer Agency Leukemia/BMT Tumour Group; September 2009.
5. Celgene REVLIMID® product monograph. Oakville, Ontario; 30 June, 2011.