BC Cancer Protocol Summary for Maintenance Therapy of Multiple Myeloma Using Lenalidomide

Protocol Code	*UMYLENMTN*
Tumour Group	*Lymphoma, Leukemia/BMT*
Contact Physician	*Dr. Kevin Song*
Contact Pharmacist	*Louisa Pang*

ELIGIBILITY:

Patients must have:

- Newly diagnosed multiple myeloma following autologous stem cell transplant,
- Minimum of stable disease post- transplant, 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.

EXCLUSIONS:

Patients must not:

- Be pregnant or lactating or
- Have a known hypersensitivity to lenalidomide or thalidomide

CAUTION:

- Platelet count less than 30 x 10^9/L
- Absolute neutrophil count (ANC) less than 1.0 x 10^9/L may be considered a relative contraindication. Consider giving filgrastim
- Creatinine Clearance less than 30 mL/min

TESTS:

- Baseline (required before first treatment): CBC & diff, platelets, creatinine, LFTs (bilirubin, ALT). 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): calcium, serum protein electrophoresis *and* serum free light chain levels, immunoglobulin panel (IgA, IgG, IgM), HBsAg, HBcoreAb, TSH
- If cytopenias a concern, every 2 weeks for the first 4 cycles: CBC and diff, platelets, creatinine, calcium

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- Every 4 weeks (required before treatment): CBC and diff, platelets, creatinine; if female of childbearing potential: quantitative beta-hCG blood test
- Every 4 weeks (required, but results do not have to be available to proceed with treatment): calcium, serum protein electrophoresis *and* serum free light chain levels
- Every 4 weeks (optional, results do not have to be available to proceed with treatment): immunoglobulin panel (IgA, IgG, IgM), urine protein electrophoresis
- 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
- If clinically indicated: bilirubin, ALT, see Precautions #2

PREMEDICATIONS:

None

SUPPORTIVE MEDICATION:

- ASA (enteric coated), warfarin, direct oral anticoagulant (DOAC) PO or low molecular weight heparin (LMWH) SC daily continuing for the duration of treatment with lenalidomide

TREATMENT:

- Start 3-4 months post stem cell transplant.

Drug	Dose	BC Cancer Administration Guideline
lenalidomide	10 mg once daily continuously (d 1-28)	PO, in the evening may be preferred

- Repeat every 28 days until progression
- At time of relapse, Compassionate Access Program (CAP) approval must be obtained to use higher doses of lenalidomide as per UMYLDREL

DOSE MODIFICATIONS:

Fatigue may respond to dose reduction

NB: Use one of the 5 mg capsules, 10 mg capsules or 15 mg capsules for dosing. The use of two 5 mg capsules for a 10 mg dose etc., does have significant budgetary implications.

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1. **Hematological:**

Initial dose	ANC (x10^9/L)	Dose
10 mg daily 28/28 days	**Day 1 of Cycle** less than 1.0	Hold until ANC greater than or equal to 1.0*, then restart; consider resuming at 10 mg daily for 21 out of 28 days
	Day 15 of Cycle† less than 1.0	Omit for remainder of cycle; restart on Day 1 of next cycle if ANC greater than or equal to 1.0*; consider resuming at 10 mg daily for 21 out of 28 days
10 mg daily *21/28 days*	**Day 1 of Cycle** less than 1.0	Hold until ANC greater than or equal to 1.0*, then restart; consider resuming at 5 mg daily for 21 out of 28 days
	Day 15 of Cycle† less than 1.0	Omit for remainder of cycle; restart on Day 1 of next cycle if ANC greater than or equal to 1.0*; consider resuming at 5 mg daily for 21 out of 28 days
5 mg	**Day 1 of Cycle** less than 1.0	Consider stopping treatment, otherwise hold until ANC greater than or equal to 1.0*, then restart
	Day 15 of Cycle† less than 1.0	Consider stopping treatment, otherwise omit for remainder of cycle; restart on Day 1 of next cycle if ANC greater than or equal to 1.0*

* follow hematology weekly
†Day 15 bloodwork for Cycle 1 to 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.
♦ may consider increasing lenalidomide dose to 15 mg daily 28/28 days after 3 months if patient is tolerating drug and ANC greater than 1.0 x 10^9/L and Platelets greater than 75 x 10^9/L

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Thrombocytopenia

Initial dose	Platelet (x10^9/L)	Dose
10 mg daily 28/28 days	**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; consider resuming at 10 mg daily *for 21 out of 28 days*.
	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*, consider resuming at 10 mg daily for *21 out of 28 days*.
10mg daily *21/28 days*	**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; consider resuming at 5 mg daily *for 21 out of 28 days*.
	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*, consider resuming at 5 mg daily *for 21 out of 28 days.*
5 mg daily *21/28 days*	**Day 1 of Cycle** less than 30	Consider 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	Consider stopping treatment; otherwise omit for remainder of cycle; restart on Day 1 of next cycle if platelet greater than or equal to 30*.

* follow hematology weekly
† Day 15 bloodwork for Cycle 1 to 4 will be monitored by the physician and physician will be responsible to check and advise patient on dose adjustment based on platelets
‡ may consider increasing lenalidomide dose to 15 mg daily 28/28 days after 3 months if patient is tolerating drug and ANC greater than 1.0 x 10^9/L and Platelets greater than 75 x 10^9/L

For females of child-bearing potential on weekly pregnancy test during cycle 1, physician will be responsible for checking results

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Renal dysfunction:

Estimated GFR (eGFR)* or Creatinine clearance (mL/min)	Dose
Less than 30	Delay and reassess in four weeks
less than 60 and greater than or equal to 30	• If currently on 10 mg daily 28/28 days consider decreasing dose to 10 mg daily *21/28 days* and reassess in four weeks to attempt to re-escalate • If currently on 10 mg daily *21/28 days* consider decreasing dose to 5 mg daily *for 21 out of 28* days and reassess in four weeks to attempt to re-escalate

*as reported in patient's laboratory report
**Further decrease in dose is not necessary for stable eGFR/Creatinine clearance greater than 30 providing other patient parameters are adequate e.g., ANC and Platelets

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. **Hepatotoxicity:** Hepatic failure, including fatal cases, have been reported in multiple myeloma patients treated with lenalidomide in combination with dexamethasone during post-marketing. The mechanism of severe drug-induced hepatotoxicity is unknown. Pre-existing viral liver disease, elevated baseline liver enzymes and concomitant medications may be risk factors. Stop lenalidomide upon elevation of liver enzymes. After return to baseline values, treatment at a lower dose may be considered.
3. **Constipation**: Patients should be warned that constipation may occur in patients taking lenalidomide.
4. **Fatigue**: Patients should be warned that lenalidomide may cause fatigue.
5. **Hypothyoidism:** 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.
6. **Venous thrombosis/embolism:** Lenalidomide with dexamethasone is known to increase the risk for thromboembolic disease. The risk is lower with lenalidomide maintenance but ASA 81mg oral daily should be considered in all patients. For those

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with higher risk of thrombo-embolic disease full anti-coagulation should be considered.

7. **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 PO daily, for the entire duration of chemotherapy and continue for one year from treatment completion for patients who are HBsAg positive and for six months for patients who are HBcoreAb positive. Such patients should also be monitored with frequent liver function tests and hepatitis B virus DNA 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.
8. **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.
9. **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. 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)

References:

1. McCarthy PL, et al. Lenalidomide after stem-cell transplantation for multiple myeloma. N Engl J Med 2012;366:1770-81.
2. Palumbo A, et al. Lenalidomide maintenance after stem-cell transplantation for multiple myeloma. N Engl J Med 2014;371:895-905.
3. Attal M, et al. Lenalidomide maintenance after stem-cell transplantation for multiple myeloma. N Engl J Med 2012;366:1782-91.

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