BCCA 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: Linda Hamata

ELIGIBILITY:
- Maintenance treatment for patients with newly diagnosed multiple myeloma, following autologous stem cell transplant
- Minimum of stable disease post transplant
- 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)

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
- Creatinine Clearance less than 30ml/min
- Known hypersensitivity to lenalidomide or thalidomide

TESTS:
- Baseline (required before first treatment): CBC & diff, platelets, creatinine, LFTs (bilirubin, AST, ALT). If female of child-bearing potential (FCBP): Confirm negative pregnancy test results 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 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,
- 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
- If clinically indicated: bilirubin, AST, ALT, see Precautions #2

PREMEDICATIONS:
None

TREATMENT:
- Start 3-4 months post stem cell transplant.

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>BCCA Administration Guideline</th>
</tr>
</thead>
<tbody>
<tr>
<td>lenalidomide</td>
<td>10 mg once daily continuously (d 1-28)</td>
<td>PO, in the evening may be preferred</td>
</tr>
</tbody>
</table>

- 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.

1. Hematological:

<table>
<thead>
<tr>
<th>Initial dose</th>
<th>ANC (x10^9/L)</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>10 mg daily 28/28 days</td>
<td>Day 1 of Cycle less than 1.0</td>
<td>Hold until ANC greater than or equal to 1.0*, then restart; consider resuming at 10 mg daily for 21 out of 28 days</td>
</tr>
<tr>
<td></td>
<td>Day 15 of Cycle † less than 1.0</td>
<td>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</td>
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<td>10 mg daily 21/28 days</td>
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<td>Consider stopping treatment, otherwise hold until ANC greater than or equal to 1.0*, then restart</td>
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<td>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*</td>
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* 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

**Thrombocytopenia**

<table>
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<tr>
<th>Initial dose</th>
<th>Platelet (x10^9/L)</th>
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<tr>
<td><strong>10 mg daily 28/28 days</strong></td>
<td>Day 1 of Cycle less than 30</td>
<td>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.</td>
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* follow hematology weekly
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‡ 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
Renal dysfunction:

<table>
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<tr>
<th>Estimated GFR (eGFR)* or Creatinine clearance (mL/min)</th>
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<tr>
<td>Less than 30</td>
<td>Delay and reassess in four weeks</td>
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<tr>
<td>less than 60 and greater than or equal to 30</td>
<td>• 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&lt;br&gt;• 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</td>
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*as reported in patient’s laboratory report<br>**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. **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.

6. **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.
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/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.

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.

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 Jan 2015

**Date revised**: 1 May 2017 (Treatment section clarified)

**References**: