Regimen Monograph

Regimen Name | Drug Regimen | Cycle Frequency | Premedication and Supportive Measures | Dose Modifications | Adverse Effects | Interactions | Drug Administration and Special Precautions | Recommended Clinical Monitoring | Administrative Information | References | Other Notes | Disclaimer

A - Regimen Name

LENA Regimen

Lenalidomide (maintenance)

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 maintenance treatment of patients with newly diagnosed multiple myeloma, following autologous stem-cell transplantation (ASCT) who have stable disease or better, with no evidence of disease progression

Supplementary Public Funding
lenalidomide
ODB Limited Use (lenalidomide - For the maintenance treatment of patients with newly diagnosed multiple myeloma, following ASCT, according to clinical criteria) (ODB Formulary)

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B - Drug Regimen

lenalidomide[1]	10 mg	PO	Daily

[1] In clinical studies after 3 months of 10 mg daily, if ANC ≥ 1 x 10^9/L, platelets ≥ 75 x 10^9/L and non-hematological toxicity ≤ Grade 1, dose escalation to 15 mg daily was permitted.

Lenalidomide 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.

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C - Cycle Frequency

CONTINUOUS TREATMENT

Until disease progression or unacceptable toxicity.

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D - Premedication and Supportive Measures

Antiemetic Regimen: Minimal – No routine prophylaxis; PRN recommended

Other Supportive Care:

Also refer to CCO Antiemetic Recommendations.

- Patients must be registered and meet all conditions of lenalidomide's controlled distribution program, including contraception.
- Prophylaxis for venous thromboembolism is recommended in patients at risk (e.g. low dose aspirin 81-100 mg PO daily or enoxaparin 40 mg SC daily)
- Careful consideration and monitoring must be taken with erythropoietin stimulating agents (ESAs), since the concomitant use of ESAs with lenalidomide may potentiate the risk of thrombosis. RBC or platelet transfusions with lenalidomide dose reductions/interruptions may be appropriate in severe / symptomatic anemia or thrombocytopenia.
- Consider G-CSF as secondary prophylaxis
- Optimal control of thyroid function is recommended prior to starting treatment

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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. Assess risk of second primary malignancies prior to starting treatment.

Dosage with toxicity

Dose levels: 10 mg daily, 5 mg daily, 5 mg daily for 21 days (out of 28 day cycle)

Hematologic Toxicity:

Dose modifications for months 1 to 3		
Maintenance dose	**Hematologic toxicity (counts x 10^9/L)**	**Action**
10 mg daily	ANC < 0.5 or platelets < 30	Hold*, restart at 5 mg daily if ANC ≥ 0.5 or platelets ≥ 30
5 mg daily	ANC < 0.5 or platelets < 30	Hold*, restart at 5 mg daily for 21 of 28 day cycle if ANC ≥ 0.5 and platelets ≥ 30
5 mg daily for 21 of 28 day cycle	ANC < 0.5 or platelets < 30	Discontinue

Dose modifications beyond month 3		
Maintenance dose	**Hematologic toxicity (counts x 10^9/L)**	**Action*** **
15 mg daily**	ANC < 0.5 or platelets < 30	Hold*, restart at 10 mg daily if ANC ≥ 0.5 or platelets ≥ 30
10 mg daily	ANC < 0.5 or platelets < 30	Hold*, restart at 5 mg daily if ANC ≥ 0.5 or platelets ≥ 30
5 mg daily	ANC < 0.5 or platelets < 30	Hold*, restart at 5 mg daily for 21 of 28 day cycle if ANC ≥ 0.5 or platelets ≥ 30
5 mg daily for 21 of 28 day cycle	ANC < 0.5 or platelets < 30	Discontinue

*Hold up to 8 weeks; if no recovery, discontinue.

** In clinical studies after 3 months of 10 mg daily, if ANC ≥ 1 x 10^9/L, platelets ≥ 75 x 10^9/L and non-hematological toxicity ≤ Grade 1, dose escalation to 15 mg daily was permitted.

*** After 3 months may re-escalate (by 1 dose level) doses reduced for hematologic toxicity if ANC ≥ 1 x 10^9/L, platelets ≥ 75 x 10^9/L for at least 1 month (McCarthy 2012)

Non-Hematologic Toxicities:

Toxicity	**Action**
Grade 2 intolerable toxicity	Decrease 1 dose level, or hold then restart at -1 dose level
Grade 3 neurotoxicity	Hold* until ≤ Grade 1, restart at -1 dose level
Grade 2 or 3 cardiac toxicity	Hold* until ≤ Grade 1, restart at -1 dose level
Grade 2 to 3 rash	Hold or consider discontinuing Discontinue if Stevens-Johnson syndrome suspected
Angioedema/ hypersensitivity, OR Grade 4 skin rash, OR Exfoliative or bullous rash, OR Suspected Stevens-Johnson syndrome, Toxic epidermal necrolysis or DRESS	Discontinue
Grade 3 other toxicity	Hold until ≤ Grade 2, restart at -1 dose level
Grade 4 toxicity	Discontinue
Pneumonitis	Hold and investigate; discontinue if confirmed
↑ LFTs	Hold until recovery to baseline level; consider restarting at a lower dose
Venous thromboembolism	Hold and restart once adequately anticoagulation is established; discontinue if recurs
Solid organ transplantation	Discontinue

*Hold up to 8 weeks; if no recovery, discontinue.

Hepatic Impairment

Population pharmacokinetics suggest no dosage adjustment is necessary in mild hepatic impairment (total bilirubin > 1 to < 1.5 x ULN or AST > ULN). No data available for moderate to severe hepatic impairment.

Renal Impairment

Lenalidomide clearance is decreased while exposure is increased in renal impairment. The following has been used in a clinical trial.

Creatinine Clearance (mL/min)	Maintenance dose
30 to <60	5mg daily
< 30 (not requiring dialysis)	5mg every other day
< 30 (requiring dialysis)	5mg 3 times a week following each dialysis

Dosage in the Elderly

The incidences of serious and non-serious adverse events are significantly higher in patients > 65 years (constipation, confusion, dyspnea, atrial fibrillation, diarrhea, fatigue, pulmonary embolism, syncope). May be related to renal impairment. Monitor geriatric patients closely, especially cardiac and renal function. Dose modification based on degree of renal impairment is required.

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F - Adverse Effects

Refer to lenalidomide drug monograph(s) for additional details of adverse effects

Very common (≥ 50%)	Common (25-49%)	Less common (10-24%)	Uncommon (< 10%), but may be severe or life-threatening
	• Fatigue • Constipation • Diarrhea • Myelosuppression +/- infection, bleeding (may be severe) • Musculoskeletal pain, headache • Edema • Cough, dyspnea • Nausea, vomiting	• Dizziness • Rash (may be severe, SJS, TEN, DRESS) • Anorexia • Blurred vision • Dyspepsia • Hyperglycemia • Abnormal electrolytes • Dysgeusia • Depression • Insomnia • Abdominal pain • Tremor	• Arterial / venous thromboembolism • Cardiotoxicity • Arrhythmia • Pneumonitis • Pancreatitis • Hypersensitivity • Hemolysis • Hepatotoxicity • Adrenal insufficiency • Tumour lysis syndrome • Secondary malignancy • Renal failure • Cholecystitis • Solid organ transplant rejection • Hyper/ hypothyroidism • Rhabdomyolysis • Syncope • Peripheral neuropathy • GVHD or transplant rejection

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G - Interactions

Refer to lenalidomide drug monograph(s) for additional details

- Lenalidomide is not a substrate, inhibitor or inducer of CYP450; co-administration with substrates or inhibitors of this enzyme is unlikely to result in significant drug interactions.
- Digoxin may increase Cmax; caution and monitor digoxin levels.
- Additive risk of thromboembolism with hormonal therapy, including contraception. Caution and monitor; consider alternative contraception and prophylaxis with anticoagulants.

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H - Drug Administration and Special Precautions

Refer to lenalidomide drug monograph(s) for additional details

Administration:

- Drug available by outpatient prescription in pharmacy registered with a controlled distribution program.
- Oral self-administration; swallow capsules whole; they should not be broken, chewed, or opened. Do not extensively handle the capsules.
- Give capsules preferably with water, either with or without food. Do not remove from blister packs until ready to take the dose. Note: Females who could become pregnant, or who plan to become pregnant can handle lenalidomide capsules if they are using latex gloves.
- If a dose is missed, it may be taken up to 12 hours after the time it is normally taken. Otherwise, skip this and take the next dose on the following day at its usual scheduled time.
- Store capsules at room temperature (15 to 30°C).

Contraindications:

- Patients with hypersensitivity (including severe rash) to lenalidomide, pomalidomide, thalidomide or any ingredient in the formulation.
- Pregnant and breastfeeding women.

- Women at risk of being pregnant and male patients who do not comply with contraception requirements (see Pregnancy section).

Other Warnings/Precautions:

- Lenalidomide contains lactose; carefully consider use in patients with hereditary galactose intolerance, severe lactase deficiency or glucose-galactose malabsorption.
- Use with caution and consider venous thromboembolism prophylaxis when used in combination with corticosteroids or thrombogenic agents, such as hormones and erythropoietin. (see adverse effects section)
- Exercise caution in patients with risk factors for arterial thromboembolism (e.g. hypertension and hyperlipidemia), or risk factors for atrial fibrillation (e.g. electrolyte abnormalities, pre-existing heart disease, hypertension, infection).
- Use with caution in patients with high tumour burden; monitor closely and use appropriate precautions for tumour lysis syndrome.

Pregnancy and Lactation:

- Lenalidomide is contraindicated in pregnancy and in females and males of childbearing potential who do not comply with the contraception conditions of the controlled drug distribution program.

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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.

Recommended Clinical Monitoring

- CBC; weekly for the first 8 weeks, then monthly
- Liver function tests; baseline and at each visit
- Renal function tests; baseline and at each visit
- Pregnancy testing requirements for women of child-bearing potential; before starting and as indicated
- Thyroid function tests; baseline and as clinically indicated

- Clinical assessments and grading of cardiac and respiratory symptoms, rash, diarrhea, fatigue, constipation, infection, bleeding, tumour lysis syndrome, arterial and venous thromboembolism, GVHD and transplant rejection (if applicable); at each visit
- Cancer screening for occurrence of secondary primary malignancy; assess risk prior to starting treatment, then at each visit or as clinically indicated
- Grade toxicity using the current NCI-CTCAE (Common Terminology Criteria for Adverse Events) version

Suggested Clinical Monitoring

- ECG; baseline, repeat if arrhythmia suspected
- INR in patients receiving warfarin; baseline and regular

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J - Administrative Information

Outpatient prescription for home administration

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K - References

Attal M, Lauwers-Cances V, Marit G, et al. Lenalidomide maintenance after stem-cell transplantation for multiple myeloma. N Engl J Med. 2012 May 10;366(19):1782-91.

Lenalidomide drug monograph, Cancer Care Ontario.

McCarthy PL, Owzar K, Hofmeister CC, et al. Lenalidomide after stem-cell transplantation for multiple myeloma. N Engl J Med. 2012;366(19):1770-81.

Palumbo A, Hajek R, Delforge M, et al. Continuous lenalidomide treatment for newly diagnosed multiple myeloma. N Engl J Med 2012;366(19):1759-69.

PEBC Advice Documents or Guidelines

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

May 2022 Updated distribution program info

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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.

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