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

Disease Site	Hematologic Myelodysplastic Syndrome (MDS)
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	Treatment of patients with symptomatic anemia due to Low- or Intermediate-1-risk MDS associated with a deletion 5q cytogenetic abnormality
Supplementary Public Funding	**lenalidomide** ODB Limited Use (lenalidomide - For the treatment of patients with anemia due to myelodysplastic syndrome (MDS), according to clinical criteria) (ODB Formulary)

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B - Drug Regimen

lenalidomide	10 mg	PO	Days 1 to 21

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

REPEAT EVERY 28 DAYS

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; clinical trials in MDS excluded patients with grade 4 neutropenia. Patients with platelets < 50 x 10^9/L should not receive lenalidomide. Assess risk of second primary malignancies prior to starting treatment.

Dosage with toxicity

Dose levels (days 1 to 21): 10mg daily, 5mg daily, 5mg every other day

Dosage with Hematologic Toxicity

Discontinue treatment if no erythroid response within 4 months of therapy initiation (less than 50% reduction in transfusion requirements or, if not transfused, less than 10 g/L rise in hemoglobin)

If myelosuppression develops **within 4** weeks of starting treatment at 10 mg daily							
Baseline Counts ($X10^9$/L)			**Counts during therapy ($X10^9$/L)**			**Action**	
Platelets		ANC*	Platelets		ANC		
≥ 100	AND/ OR	≥ 1	< 50	AND/ OR	<0.75	Hold	Restart at 5mg/day when platelets ≥ 50 and ANC ≥ 1
≥60 to <100		<1	↓ 50% of baseline		<0.50	Hold	Restart at 5mg/day when platelets ≥ 50 and ANC ≥ 0.5
< 60**						Hold	Restart at 5mg/day when platelets ≥ 30 and ANC ≥ 0.5

**ANC= Absolute Neutrophil Counts*

*** Clinical trial excluded patients with platelets < 50 x 10^9/L or grade 4 ANC.*

If myelosuppression develops **after 4** weeks of starting treatment at 10 mg daily				
Counts during therapy ($X10^9$/L)			Action	
Platelets		ANC		
<30, or <50 requiring transfusion	AND/ OR	<0.5 ≥ 7 days or with fever (≥38.5°C)	Hold	Restart at 5mg/day when platelets ≥ 30 (without bleeding) and ANC ≥ 0.5

If myelosuppression develops during treatment at **5mg** daily				
Counts during therapy ($X10^9$/L)			Action	
Platelets		ANC		
<30, or <50 requiring transfusion	AND/ OR	<0.5 ≥ 7 days or with fever (≥38.5^oC)	Hold	Restart at 5mg/ **EVERY OTHER DAY** when platelets ≥ 30 (without bleeding) and ANC ≥ 0.5

Non-Hematologic Toxicities

Toxicity	Action
≥Grade 3 non-hematological	Hold; restart with ↓ 1 dose level when ≤Grade 2
Grade 2 to 3 rash	Hold or consider discontinuing Discontinue if Stevens-Johnson syndrome suspected
↑ LFTs	Hold Consider restarting at a lower dose when ≤ baseline levels
Pneumonitis	Hold and investigate if suspected; discontinue if confirmed
Angioedema, OR Grade 4 skin rash, OR Exfoliative or bullous rash, OR Suspected Stevens-Johnson Syndrome, Toxic epidermal necrolysis or DRESS	Discontinue
Solid organ transplant rejection	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.

Creatinine Clearance (mL/min)	Starting dose in MDS patients
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	• Arterial / venous thromboembolism • Cardiotoxicity • Arrhythmia • Pneumonitis • Pancreatitis • Hypersensitivity • Hemolysis • Hepatotoxicity • Adrenal insufficiency • Tumour lysis

		• Insomnia • Abdominal pain • Tremor	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.
- MDS patients with platelet counts < 50 x 10^9/L. MDS patients with grade 3 or 4 thrombocytopenia or grade 4 neutropenia were excluded from clinical trials.
- 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.
- Use with caution and monitor closely in patients with previous viral infections such as HBV and herpes zoster.

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 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; baseline, weekly for first 8 weeks, then monthly
- Liver function tests; baseline and at each visit
- Renal function tests; baseline and at each visit; increased frequency in patients 65 years or older
- Pregnancy testing requirements for women of child-bearing potential; before starting and as indicated
- Thyroid function tests; baseline and ongoing
- Clinical assessments and grading of cardiac and respiratory symptoms, rash, diarrhea, fatigue, constipation, infection, bleeding, tumour lysis syndrome, arterial and venous thromboembolism, GVHD or organ 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 as clinically indicated

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J - Administrative Information

Outpatient prescription for home administration

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K - References

Fenaux P, Giagounidis A, Selleslag D, et al. A randomized phase 3 study of lenalidomide versus placebo in RBC transfusion-dependent patients with Low-/Intermediate-1-risk myelodysplastic syndromes with del5q. Blood 2011;118(14):3765-76.

Lenalidomide drug monograph, Cancer Care Ontario.

List A, Dewald G, Bennett J, et al. Lenalidomide in the myelodysplastic syndrome with chromosome 5q deletion. N Engl J Med 2006;355:1456-65.

List A, Kurtin S, Roe DJ, et al. Efficacy of lenalidomide in myelodysplastic syndromes. N Engl J Med 2005;352:549-57.

PEBC Advice Documents or Guidelines

- Systemic therapy for the treatment of adult patients with lower-risk myelodysplastic syndromes

May 2022 Updated distribution program info

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M - Disclaimer

Regimen Abstracts

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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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