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

RUXO Regimen

Ruxolitinib

Disease Site

Hematologic
Myeloproliferative Neoplasms (MPNs)

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 the treatment of splenomegaly and/or its associated symptoms in adult patients with primary myelofibrosis (also known as chronic idiopathic myelofibrosis), post-polycythemia vera myelofibrosis or post-essential thrombocythemia myelofibrosis.
- For the control of hematocrit in adult patients with polycythemia vera (PV) resistant to or intolerant of a cytoreductive agent.

Supplementary Public Funding

ruxolitinib
Exceptional Access Program (ruxolitinib - For patients with intermediate to high risk symptomatic myelofibrosis, or patients with symptomatic splenomegaly, according to specific criteria) (EAP Website)

ruxolitinib
Exceptional Access Program (ruxolitinib - For the treatment of patients with polycythemia vera according to criteria.) (EAP Website)

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B - Drug Regimen

ruxolitinib

Starting dose is based on indication, platelet and neutrophil counts, and degree of hepatic or renal impairment.

Treatment should not be started until neutrophils are ≥ 1 x 10^9/L and platelets ≥ 50 x 10^9/L.

ANC (x10^9/L)	Platelet Count (x10^9/L)	Starting Dose Myelofibrosis	Starting Dose Polycythemia Vera
> 1	> 200	20 mg PO twice daily	10 mg PO twice daily
> 1	100 - 200	15 mg PO twice daily	10 mg PO twice daily
> 1	75 - 99	10 mg PO twice daily	5 mg PO twice daily
> 1	50 - 74	5 mg PO twice daily	5 mg PO twice daily
≤ 1	< 50	Do not use	Do not use

Refer to section E for dose titrations, if applicable.

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C - Cycle Frequency

CONTINUOUS TREATMENT

Until disease progression or unacceptable toxicity; must be discontinued after 6 months if no evidence of improvement in symptoms or spleen size (MF) or after 16 months if no clinical benefit (PV).

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D - Premedication and Supportive Measures

Antiemetic Regimen: Minimal – No routine prophylaxis; PRN recommended

Other Supportive Care:

- **Screen for hepatitis B virus in all cancer patients starting systemic treatment.** Refer to the hepatitis B virus screening and management guideline.
- Perform tuberculosis skin test and/or Interferon-gamma release assay before treatment initiation. Caution with interpreting results in severely immunocompromised patients due to possible false negatives.
- Patients should minimize exposure to risk factors for skin cancer such as exposure to sunlight.
- Also refer to CCO Antiemetic Recommendations.

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E - Dose Modifications

Doses should be modified according to the protocol by which the patient is being treated.

Titration of Dose

If response to treatment is inadequate, escalation may proceed as detailed below. The **maximum** dose is 25 mg PO BID.

The starting dose should not be increased within the first 4 weeks of treatment (for patients with MF) and 8 weeks of treatment (for PVD).

Discontinue after 6 months if no evidence of improvement in symptoms or spleen size (MF) or after 16 months if no clinical benefit (PV).

ANC		Platelets (x 10^9/L)	At 4 weeks (MF), or 8 weeks (PV)	Every 2 weeks (or more) thereafter
>0.75	AND	>125 (and nadir >100)	↑ by 5mg bid	↑ by 5mg bid, if blood counts criteria are met.
≤0.75	OR	≤ 125 (or nadir < 100)	Do not escalate.	Do not escalate.

Dosage with toxicity

Toxicity (x 10^9/L)	Action
Hb < 80 g/L (PV pts only)	Hold; when recovered, may restart at 5 mg PO twice daily and titrate gradually.
Hb < 120 g/L (PV pts only)	Consider dose reduction, especially if Hb < 100 g/L.
Platelets < 50 or ANC < 0.5	Hold; when platelet and ANC counts above these levels, may restart at 5 mg PO twice daily and titrate gradually.
Platelets 50 to < 125 (MF pts only)	Refer to Dose Modification for Thrombocytopenia table below to minimize holds. May titrate gradually if appropriate.
PML, active tuberculosis, severe infection	Hold and investigate; discontinue if confirmed.
Bleeding requiring intervention (regardless of platelet count)	Hold until event is resolved; consider restart at previous dose if cause of bleeding controlled. If the underlying cause persists, consider restart at a lower dose.

Dose Modification for Thrombocytopenia (MF)

	Dose at Time of Platelet Decline				
Platelet count	**25 mg BID**	**20 mg BID**	**15 mg BID**	**10 mg BID**	**5 mg BID**
	New dose	**New dose**	**New dose**	**New dose**	**New dose**
100 to < 125	20 mg BID	15 mg BID	No change	No change	No change
75 to < 100	10 mg BID	10 mg BID	10 mg BID	No change	No change
50 to < 75	5 mg BID	5 mg BID	5 mg BID	5 mg BID	No change

Hepatic Impairment

Avoid use in patients with hepatic impairment and platelets < 100 x 10^9/L.

Hepatic impairment	Ruxolitinib Dose (MF or PV)
None	No adjustment required.
Any degree	Start at 50% of usual dose*. Monitor carefully and adjust as appropriate.

*round up to the nearest dosage strength, if necessary.

Renal Impairment

Avoid use in patients with moderate to severe renal impairment if platelets < 100 x 10^9/L.

Hemodialysis is not expected to enhance the elimination of ruxolitinib.

Renal Impairment	Ruxolitinib Dose (MF or PV)
Mild	No adjustment required.
Moderate (CrCl 30-50 mL/min)	Start at 50% of usual dose*. Monitor closely for toxicity. Avoid if platelets < 100 x 10^9/L.
Severe (CrCl < 30 mL/min)	
Patients on hemodialysis	Single dose given only after each dialysis session based on platelet count. **MF**: 15 mg for platelets 100-200 x 10^9/L; 20mg for platelets > 200 x 10^9/L **PV**: 10 mg

*round up to the nearest dosage strength, if necessary

Dosage in the elderly:

No dosage adjustments required. No overall differences in safety or effectiveness were observed between patients ≥ 65 years of age and younger patients with MF or PV.

Dosage based on gender:

Female MF patients may be at a higher risk of anemia than male patients. Ruxolitinib clearance in women with MF was lower compared to men, however, no specific dose adjustment has been recommended.

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F - Adverse Effects

Refer to 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
• Myelosuppression ± infection, bleeding (may be severe, includes atypical infections (fungal, viral, TB), viral reactivation and endocarditis)	• ↑ LFTs • Hyperlipidemia	• Dizziness • Headache • Diarrhea • Musculoskeletal pain • Weight gain • Cough, dyspnea	• Angina • Bradycardia • Prolonged PR interval • Venous thromboembolism • PML • Secondary malignancy • Withdrawal syndrome

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G - Interactions

Refer to ruxolitinib drug monograph(s) for additional details.

- Decrease ruxolitinib dose by 50% with concomitant use of strong CYP3A4 inhibitors
  - Monitor more frequently for cytopenias (e.g., twice a week) when starting a strong CYP3A4 inhibitor
  - Avoid concomitant use with ruxolitinib if platelets < 100
- Monitor for cytopenias with concomitant use of moderate CYP3A4 inhibitors.
- Decrease ruxolitinib dose by 50% if used with combined moderate CYP2C9 and CYP3A4 inhibitors (e.g. fluconazole); avoid fluconazole at doses > 200mg daily
  - Monitor more frequently for cytopenias (e.g., twice a week) when starting combined moderate CYP2C9 and CYP3A4 inhibitors
  - Avoid concomitant use with ruxolitinib if platelets < 100
- If possible, avoid drugs that decrease heart rate and/or prolong the PR interval due to increased risk of bradycardia.

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H - Drug Administration and Special Precautions

Refer to ruxolitinib drug monograph(s) for additional details.

Administration

- Administer with or without food with a glass of water.
- The tablets should be swallowed whole; do not cut, break, dissolve, crush or chew the tablets.
- Avoid grapefruit, starfruit, Seville oranges, their juices or products during treatment.
- If a dose is missed, skip this dose and take the next dose as scheduled. Do not double the dose to make up for the missed one.
- Store at room temperature (15-25°C).

Contraindications

- Patients who have a hypersensitivity to this drug or any of its components
- Patients who have/had progressive multifocal leukoencephalopathy (PML)

Warnings/Precautions

- Major adverse cardiovascular events (MACE), arterial/venous thrombosis, and/or malignancy, including fatal outcomes, have been reported with the JAK inhibitor tofacitinib. Consider the benefits and risks prior to initiating, or continuing, therapy of JAK inhibitors, especially in patients > 65 years, who are current or past smokers, or with other cardiovascular, thrombosis or malignancy risk factors.
- Ruxolitinib can cause bradycardia and prolongation of PR interval; use with caution in patients on drugs with similar effects or with history of cardiovascular disease including bradycardia, syncope or arrhythmia, sick sinus syndrome, sinoatrial block, atrioventricular (AV) block, ischemic heart disease, or congestive heart failure.
- Serious bacterial, mycobacterial, fungal, and viral infections including viral reactivation and opportunistic infections (in some cases fatal) have been reported. Do not administer ruxolitinib in patients with active tuberculosis or active serious infections.
- Contains lactose and should not be used in patients with hereditary lactase/glucose or galactose disorders

Pregnancy/Lactation

- This regimen is not recommended for use in pregnancy. Adequate contraception should be used by patients and their partners while on treatment and after the last treatment dose. Recommended methods and duration of contraception may differ depending on the treatment. Refer to the drug monograph(s) for more information.
- Breastfeeding is not recommended during this treatment and after the last treatment dose. Refer to the drug monograph(s) for recommendations after the last treatment dose (if available).
- Fertility effects: Probable

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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.

Refer to the hepatitis B virus screening and management guideline for monitoring during and after treatment.

Recommended Clinical Monitoring

- CBC; baseline, every 2 - 4 weeks until doses are stabilized, and then as clinically indicated. Monitor more frequently for cytopenias (e.g., twice a week) when starting a strong CYP3A4 inhibitor or combined moderate CYP2C9 and CYP3A4 inhibitors.
- Liver and renal function tests; baseline and as clinically indicated
- Lipid monitoring; prior to starting, 4 weeks after starting, then as clinically indicated
- Pulse rate and blood pressure; baseline and as clinically indicated
- ECG; baseline and as clinically indicated
- Clinical toxicity assessment for cardiovascular effects, infections (including ocular), bleeding, thrombosis, skin effects (including malignancies) and withdrawal syndrome (if applicable); at each visit
- Grade toxicity using the current NCI-CTCAE (Common Terminology Criteria for Adverse Events) version

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J - Administrative Information

Outpatient prescription for home administration

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K - References

Ruxolitinib drug monograph, Ontario Health (Cancer Care Ontario).

Harrison C, Kiladjian J, Kathrin Al-Ali H, et al. JAK inhibition with ruxolitinib versus best available therapy for myelofibrosis. N Engl J Med 2012;366-787-98.

Tefferi A and Pardanani A. Serious adverse events during ruxolitinib treatment discontinuation in patients with myelofibrosis. Mayo Clinic Proceedings 2011;86(12):1188-91.

Verstovsek S, Mesa RA, Gotlib J, et al. A double-blind placebo-controlled trial of ruxolitinib for myelofibrosis. N Engl J Med 2012;366:799-807.

March 2025 Updated Pregnancy/lactation section

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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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