Myolop™

Ruxolitinib Phosphate INN

Composition:

Myolop™ 5 Tablet: Each tablet contains Ruxolitinib Phosphate INN equivalent to Ruxolitinib 5 mg.
Myolop™ 10 Tablet: Each tablet contains Ruxolitinib Phosphate INN equivalent to Ruxolitinib 10 mg.

Pharmacology:

Ruxolitinib, a kinase inhibitor, inhibits Janus Associated Kinases (JAKs) JAK1 and JAK2 which mediate the signaling of a number of cytokines and growth factors that are important for hematopoiesis and immune function. JAK signaling involves recruitment of STATs (signal transducers and activators of transcription) to cytokine receptors, activation and subsequent localization of STATs to the nucleus leading to modulation of gene expression.

Indications:

1. Intermediate or high-risk myelofibrosis, including primary myelofibrosis, post-polycythemia vera myelofibrosis and post-essential thrombocythemia myelofibrosis in adults.
2. Polycythemia vera in adults who have had an inadequate response to or are intolerant of hydroxyurea.
3. Steroid-refractory acute graft-versus-host disease in adult and pediatric patients 12 years and older.
4. Chronic graft-versus-host disease after failure of one or two lines of systemic therapy in adult and pediatric patients 12 years and older.

Dose & administration:

Myelofibrosis: The recommended starting dose of Ruxolitinib is based on platelet count. A complete blood count (CBC) and platelet count must be performed before initiating therapy, every 2 to 4 weeks until doses are stabilized, and then as clinically indicated. Doses may be titrated based on safety and efficacy.

Platelet Count	Starting Dose
>200 × 10^9/L	20 mg orally twice daily
100 × 10^9/L to 200 × 10^9/L	15 mg orally twice daily
50 × 10^9/L to <100 × 10^9/L	5 mg orally twice daily

Polycythemia Vera: The recommended starting dose of Ruxolitinib is 10 mg twice daily. Doses may be titrated based on safety and efficacy.

Acute Graft-Versus-Host Disease: The recommended starting dose of Ruxolitinib is 5 mg given orally twice daily. Consider increasing the dose to 10 mg twice daily after at least 3 days of treatment if the ANC and platelet counts are not decreased by 50% or more relative to the first day of dosing with Ruxolitinib.

Chronic Graft-Versus-Host Disease: The recommended starting dose of Ruxolitinib is 10 mg given orally twice daily

Thrombocytopenia: Hold Ruxolitinib regardless of platelet count for bleeding that requires intervention. In this situation, treatment may be resumed once bleeding has resolved.

Baseline platelet count of 100 X 10^9 cells/L or higher:

- Current platelet count of 125 X 10^9 cells/L or higher: No dose adjustment
- Current platelet count of 100 to 124 X 10^9 cells/L: Decrease dose by 5 mg twice daily; no dose adjustment if original dose was 15 mg twice daily or less.
- Current platelet count of 75 to 99 X 10^9 cells/L: Decrease dose to 10 mg twice daily; no dose adjustment if original dose was 10 mg twice daily or less.
- Current platelet count of 50 to 74 X 10^9 cells/L: Decrease dose to 5 mg twice daily; no dose adjustment if original dose was 5 mg twice daily.
- Current platelet count of less than 50 X 10^9 cells/L: Hold Ruxolitinib. May restart treatment (dose dependent on platelet count) when platelets recover to greater than 50 X 10^9 cells/L. *Baseline platelet count of 50 to 99 X 10^9 cells/L:*
- Current platelet count of 25 to 35 X 10^9 cells/L and platelet decline during prior 4 weeks is less than 20%: Decrease total daily dose by 5 mg; for patients on 5 mg daily before platelet decline, continue same dose.
- Current platelet count of less than 25 X 10^9 cells/L: Hold ruxolitinib. May restart therapy when platelets greater than 35 X 10^9 cells/L, starting with a dose at least 5 mg twice daily less than the dose when held, or 5 mg daily (whichever is less).

Neutropenia: For an absolute neutrophil count (ANC) of less than 0.5 X 10^9 cells/L: Hold Ruxolitinib.

Hematologic Toxicity:

- Hemoglobin level of 12 grams/dL or higher AND a platelet count of 100 X 10^9 cells/L or higher: No dosage adjustment required.
- Hemoglobin level of 10 to 11 grams/dL AND a platelet count of 75 to 99 X 10^9 cells/L: Consider a dosage reduction.
- Hemoglobin level of 8 to 9 grams/dL or a platelet count of 50 to 74 X 10^9 cells/L: Reduce the current Ruxolitinib dosage by 5 mg twice daily; if the current dosage is 5 mg twice daily, reduce the dosage to 5 mg once daily.
- Hemoglobin level of less than 8 grams/dL or a platelet count of less than 50 X 10^9 cells/L or an ANC of less than 1 X 10^9 cells/L: Hold Ruxolitinib until hematologic parameters are recovered to acceptable levels.

Graft-Versus-Host Disease (GVHD):

Clinically significant thrombocytopenia after supportive measures: Reduce the current Ruxolitinib dosage by 5 mg twice daily; if the current dosage is 5 mg twice daily, reduce the dosage to 5 mg once daily. Resume therapy at the prior dosage when the platelet counts recover to previous values.

ANC less than 1 X 10^9 cells/L (considered related to therapy): Hold Ruxolitinib for up to 14 days and then resume at a reduced dosage (i.e., from 10 mg twice daily to 5 mg twice daily or from 5 mg twice daily to 5 mg once daily).

Dosage Adjustments with strong CYP3A4 inhibitors or fluconazole doses 200 mg or less (Myelofibrosis or PolycythemiaVera): Avoid the use of Ruxolitinib with Fluconazole doses greater than 200 mg/day. *Stable on Ruxolitinib 10 mg PO twice daily or more.* Reduce Ruxolitinib dose by 50%, rounding up to the closest available tablet strength. *Stable on Ruxolitinib 5 mg PO twice daily:* Reduce Ruxolitinib dose to 5 mg PO once daily. *Stable on Ruxolitinib 5 mg PO once daily:* Avoid the use of strong CYP3A4 inhibitors or fluconazole treatment.

Contra-indication:

None

Warning and precaution:

Thrombocytopenia, Anemia and Neutropenia: Treatment with Ruxolitinib can cause thrombocytopenia, anemia and neutropenia. Manage thrombocytopenia by reducing the dose or temporarily interrupting Ruxolitinib. Platelet transfusions may be necessary. Patients developing anemia may require blood transfusions and/or dose modifications of Ruxolitinib.
Risk of Infection: Serious bacterial, mycobacterial, fungal and viral infections have occurred. Delay starting therapy with Ruxolitinib until active serious infections have resolved.
Non-Melanoma Skin Cancer (NMSC): Non-melanoma skin cancers including basal cell, squamous cell, and Merkel cell carcinoma have occurred in patients treated with Ruxolitinib. Perform periodic skin examinations.
Lipid Elevations: Treatment with Ruxolitinib has been associated with increases in lipid parameters including total cholesterol, low-density lipoprotein (LDL) cholesterol and triglycerides.
Major Adverse Cardiovascular Events (MACE): JAK-inhibitor has increased the risk of MACE, including cardiovascular death, myocardial infarction and stroke (compared to those treated with TNF blockers) in patients with rheumatoid arthritis, a condition for which Ruxolitinib is not indicated.
Secondary Malignancies: JAK-inhibitor has increased the risk of lymphoma and other malignancies excluding NMSC (compared to those treated with TNF blockers) in patients with rheumatoid arthritis, a condition for which Ruxolitinib is not indicated. Patients who are current or past smokers are at additional increased risk.

Side effects:

Common: Anemia, Thrombocytopenia, Neutropenia, Hypercholesterolemia, Elevated-AST, ALT, Lipase, Amylase & Creatinine, Infections, Musculoskeletal pain, Hemorrhage, Hypertension, Pyrexia, Edema, Fatigue, Dyspnea, Thrombosis, Diarrhea, Rash & Headache.
Rare: Constipation, Weight Gain, Nausea, Herpes Zoster & Urinary Tract Infections.

Use in specific populations:

Pregnancy: There are no studies with the use of Ruxolitinib in pregnant women to inform drug-associated risks.

Lactation: No data are available regarding the presence of Ruxolitinib in human milk, the effects on the breast fed child, or the effects on milk production.

Pediatric Use: The safety and effectiveness of Ruxolitinib for treatment of myelofibrosis or polycythemia vera in pediatric patients have not been established. The safety and effectiveness of Ruxolitinib for treatment of steroid-refractory aGVHD has been established for treatment of children 12 years and older.

Geriatric Use: No overall differences in safety or effectiveness of Ruxolitinib were observed between geriatric patients and younger patients.

Hepatic Impairment: Exposure of Ruxolitinib increased with mild (Child-Pugh A), moderate (Child-Pugh B) and severe (Child-Pugh C) hepatic impairment. Reduce Ruxolitinib dosage as recommended in patients with MF, PV & cGVHD with hepatic impairment.

Renal Impairment: Total exposure of Ruxolitinib and its active metabolites increased with moderate (CLcr 30 to 59 mL/min) and severe (CLcr 15 to 29 mL/min) renal impairment and ESRD (CLcr less than 15 mL/min) on dialysis. Modify Ruxolitinib dosage as recommended.

Drug interaction:

Fluconazole: Concomitant use of Ruxolitinib with fluconazole increases Ruxolitinib exposure which may increase the risk of exposure-related adverse reactions.

Strong CYP3A4 Inhibitors: Concomitant use of Ruxolitinib with strong CYP3A4 inhibitors increases Ruxolitinib exposure, which may increase the risk of exposure-related adverse reactions. Reduce the Ruxolitinib dosage when used concomitantly with strong CYP3A4 inhibitors except in patients with aGVHD or cGVHD.

Strong CYP3A4 Inducers: Concomitant use of Ruxolitinib with strong CYP3A4 inducers may decrease Ruxolitinib exposure, which may reduce efficacy of Ruxolitinib. Monitor patients frequently and adjust the Ruxolitinib dose based on safety and efficacy.

Overdose:

There is no known antidote for overdoses with Ruxolitinib. Single doses up to 200 mg have been given with acceptable acute tolerability.

Storage:

Store in a cool and dry place below 30°C, protect from light & moisture. Keep the medicine out of reach of children.

Packing:

Myolop™ 5 Tablet: Each box contains 28 tablets and one packet silica gel in a sealed HDPE container.
Myolop™ 10 Tablet: Each box contains 28 tablets and one packet silica gel in a sealed HDPE container.

Manufactured by:
Jenphar Bangladesh Ltd.
Sreepur, Gazipur, Bangladesh.

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