ruxolitinib (rux-oh-li-tinib)

Classification
Therapeutic: antineoplastics
Pharmacologic: kinase inhibitors

Pregnancy Category C

Indications
Treatment of intermediate- or high-risk myelofibrosis (including primary myelofibrosis, post-polycythemia vera myelofibrosis and post-essential thrombocytopenia fibrosis).

Action
Inhibits kinases involved in the signaling of hematopoiesis and immune processes.

Therapeutic Effects:
Decrease in mutant cells in the spleen, decreased circulating inflammatory cells and decreased spleen size.

Pharmacokinetics
Absorption: Well absorbed (95%) following oral administration.
Distribution: Unknown.
Protein Binding: 97%.
Metabolism and Excretion: Mostly metabolized (99%) in the liver (CYP3A4 enzyme system). Some metabolites have pharmacologic activity and account for 18% of action. Metabolites are excreted in urine (74%) and feces (22%).
Half-life: Ruxolitinib—3 hr; Ruxolitinib plus metabolites—5.8 hr.

TIME/ACTION PROFILE (blood levels)
ROUTE ONSET PEAK DURATION
PO unknown 1–2 hr 12 hr

Contraindications/Precautions
Contraindicated in: Severe renal impairment (CCr < 15 mL/min); Concurrent use of strong CYP3A4 inhibitors and platelet count of 100 × 10^9/L; Breastfeeding should be avoided.

Use Cautiously in: Hepatic/moderate renal impairment (dose reduction recommended); OB: Use during pregnancy only if potential benefit justifies potential fetal risk; PO: Safely and effectively use not established.

Adverse Reactions/Side Effects
CNS: PROGRESSIVE MULTIFOCAL LEUKOENCEPHALOPATHY, dizziness, headache, herpes zoster.
Derm: ecchymoses.
Hemat: anemia, thrombocytopenia, neutropenia.

Interactions
Drug-Drug: Concurrent use of strong inhibitors of the CYP3A4 enzyme system including boceprevir, clarithromycin, conivaptan, indinavir, itraconazole, ketoconazole, lopinavir/ritonavir, nefazodone, nelfinavir, posaconazole, ritonavir, saquinavir, telaprevir, telithromycin, and voriconazole may increase blood levels and effects; initial dose should be reduced.

Drug-Food: Concurrent use with grapefruit juice may increase levels and effects; initial dose should be reduced.

Route/Dosage
PO (Adults):
Platelet count < 200 × 10^9/L—20 mg twice daily initially, dose based on response to a maximum of 25 mg twice daily; Platelet count between 100 × 10^9/L and 200 × 10^9/L—15 mg twice daily initially; dose based on response to a maximum of 25 mg twice daily; Platelet count between 50 × 10^9/L and 99 × 10^9/L—5 mg twice daily initially; dose may be increased by 5 mg twice daily; no increments should be made in the first 4 wk and then may be made every 2 wk.

Renal Impairment
PO (Adults):
CCr 15–59 mL/min and platelet count between 100 × 10^9/L and 150 × 10^9/L—10 mg twice daily initially; CCr 15–59 mL/min and platelet count < 50 × 10^9/L—Avoid; CCr < 15 mL/min (on dialysis) and platelet count between 100 × 10^9/L and 150 × 10^9/L—15 mg after dialysis; CCr < 15 mL/min (on dialysis) and platelet count between 50 × 10^9/L and 100 × 10^9/L—20 mg after dialysis; CCr < 15 mL/min (on dialysis) and platelet count between < 50 × 10^9/L—20 mg after dialysis.

Hepatic Impairment
PO (Adults): Platelet count between 100 × 10^9/L and 150 × 10^9/L—10 mg twice daily initially.
2 NURSING IMPLICATIONS

Assessment

● Assess for signs and symptoms of infection (fever, dyspnea, chills, sore throat) prior to and periodically during therapy.

● Assess for new signs or symptoms suggestive of PML, an opportunistic infection of the brain caused by the JC virus, leading to death or severe disability; withhold dose and notify health care professional promptly.

Monitor during therapy and for at least 6 months following discontinuation. PML symptoms may begin gradually but usually worsen rapidly. Symptoms vary depending on which part of the brain is infected (mental function declines rapidly and progressively, causing dementia; speaking becomes increasingly difficult; partial blindness; difficulty walking; rashes, headaches and seizures occur). Diagnosis is usually made via gadolinium-enhanced MRI and CSF analysis. Risk of PML increases with the number of infusions. Withhold exsufflation at first signs of PML.

● Monitor for signs and symptoms of herpes zoster infection (skin lesions, tingling and burning of skin) prior to and periodically during therapy.

Lab Test Considerations: Monitor CBC and platelet count prior to initiating therapy, every 2–4 wks until doses are stabilized, and then as clinically indicated. Patients with platelet counts of $\leq 200 \times 10^9$ at start of therapy are more likely to develop thrombocytopenia.

● If platelet count $\leq 50 \times 10^9$ or ANC $\leq 0.5 \times 10^9$ on any day, interrupt therapy. May restart therapy if platelet count returns to $\geq 75 \times 10^9$ or ANC $\geq 1.0 \times 10^9$ with dose of 5 mg twice daily or 1 mg twice daily below largest dose in week prior to treatment interruption. Maximum restart dose: if platelet count returns to $\geq 125 \times 10^9$ or ANC $\geq 1.5 \times 10^9$, restart at $50 \times 10^9$ twice daily. If platelet count returns to $\leq 125 \times 10^9$, restart at $25 \times 10^9$ twice daily.

Potential Nursing Diagnoses

Risk for infection (Adverse Reactions)

Implementation

● PO: Administer without regard to food.

● Tablets may be suspended in 40 mL of water and stir for 10 min. Wait 6–8 hr before tablet is dispersed; suspension can be administered through an NG tube using a syringe. Rinse tube with 75 mL of water.

● Tablets should be administered following dialysis for patients requiring dialysis.

Patient/Family Teaching

● Instruct patient to take medication as directed. If a dose is missed, omit and take next dose at prescribed time; do not double doses. When discontinuing therapy, reduce dose gradually by 5 mg twice daily each wk. If therapy is discontinued, signs and symptoms of myelofibrosis are expected to return.

● Instruct patient to avoid drinking grapefruit juice during therapy; may affect blood levels of ruxolitinib.

● Advise patient to notify health care professional promptly if signs and symptoms of infection, PML, herpes zoster occur. Diagnosis is usually made via gadolinium-enhanced MRI and CSF analysis. Risk of PML increases with the number of infusions. Withhold exsufflation at first signs of PML.

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● Advise patient to notify health care professional if pregnancy is planned or suspected, or if breast feeding. Advise patient to avoid breast feeding during therapy.

● Advise patient of the need for frequent blood tests to monitor for adverse reactions.

Evaluation/Desired Outcomes

Decrease in spleen size and/or spleen volume. If efficacy is insufficient and platelet and neutrophil counts are adequate, doses may be increased by 5 mg twice daily increments to 25 mg twice daily.

Why was this drug prescribed for your patient?