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Momelotinib (Ojjaara®) for the Management of Myelofibrosis-Associated Anemia

Description: This PQI outlines key clinical considerations for the management of patients receiving momelotinib for myelofibrosis (MF)-associated anemia.

Background: Momelotinib is an oral Janus kinase (JAK) inhibitor with activity against JAK1, JAK2, and activin A receptor type 1 (ACVR1). Inhibition of ACVR1 leads to decreased liver hepcidin expression and increased iron availability, which may contribute to increased red blood cell production.[1]

FDA-Approved Indication:[1]

- Treatment of intermediate or high-risk MF, including primary MF and secondary MF (post-polycythemia vera and post-essential thrombocythemia), in adults with anemia.

Common Adverse Reactions and Laboratory Abnormalities (≥20%):

- Thrombocytopenia, diarrhea, hemorrhage, bacterial infection, fatigue, dizziness, and nausea.[1]

Paresthesia was reported in 8% of patients receiving momelotinib in MOMENTUM (Grade ≥ 3, 1%).[1,2]

Additional clinically significant risks requiring monitoring or evaluation include:

- Serious infections and HBV reactivation, neutropenia, hepatotoxicity, severe cutaneous adverse reactions (SCARs), major adverse cardiovascular events (MACE), thrombosis, and secondary malignancies.[1]

PQI Process:

1. **Verify Patient Eligibility**
   - Confirm adult patient with intermediate- or high-risk MF, including primary MF or secondary MF (post-PV or post-ET), with anemia[1]

   Additional Practice-Based Considerations:
   - Symptomatic splenomegaly and/or constitutional symptoms
   - Transfusion dependence or worsening anemia
   - Prior JAK-inhibitor intolerance due to anemia
   - Baseline thrombocytopenia and anemia

2. **Baseline Assessment**

   Per Prescribing Information:[1]
   - Obtain CBC, including platelet and neutrophil counts.
   - Obtain hepatic panel.
   - Assess for active infection; delay initiation until active infection resolved.
   - In patients with hepatitis B virus (HBV) infection, check hepatitis B serologies.

   Additional Practice-Based Considerations
   - Assess baseline anemia and transfusion requirements/history.
   - Assess constitutional symptom burden and spleen size.

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- Complete medication reconciliation and drug interaction review.
- Assess comprehensive metabolic panel (CMP)/renal function as clinically indicated.
- Consider HBV screening based on institutional practice and patient risk factors.

3. **Dosage and Administration**[1]
   - Recommended dose: 200 mg orally once daily.
   - For patients with severe hepatic impairment (Child-Pugh Class C), the recommended dose is 150 mg once daily. No dosage adjustment is recommended for mild or moderate hepatic impairment.
   - May be taken with or without food.
   - Swallow tablets whole; do not cut, crush, or chew.
   - If a dose is missed, skip the missed dose and take the next scheduled dose the following day.

4. **Dosage Modifications**[1]
   - Dose modifications may be required for thrombocytopenia, neutropenia, hepatotoxicity, and other Grade 3 or higher nonhematologic toxicities.

Adverse Reaction	Criteria	Recommended Dose Modification
Thrombocytopenia	Baseline platelets ≥100 × 10^9/L and current platelets 20 × 10^9/L to <50 × 10^9/L	Reduce daily dose by 50 mg from the last given dose
Thrombocytopenia	Baseline platelets ≥100 × 10^9/L and current platelets <20 × 10^9/L	Interrupt treatment until platelets recover to ≥50 × 10^9/L. Restart at a daily dose 50 mg below the last given dose
Thrombocytopenia	Baseline platelets ≥50 × 10^9/L to <100 × 10^9/L and current platelets <20 × 10^9/L	Interrupt treatment until platelets recover to ≥50 × 10^9/L. Restart at a daily dose 50 mg below the last given dose
Thrombocytopenia	Baseline platelets <50 × 10^9/L and current platelets <20 × 10^9/L	Interrupt treatment until platelets recover to baseline. Restart at a daily dose 50 mg below the last given dose
Neutropenia	ANC <0.5 × 10^9/L	Interrupt treatment until ANC ≥0.75 × 10^9/L. Restart at a daily dose 50 mg below the last given dose
Hepatotoxicity	ALT and/or AST >5 × ULN (or >5 × baseline if baseline abnormal) and/or total bilirubin >2 × ULN (or >2 × baseline if baseline abnormal)	Interrupt treatment until AST/ALT ≤2 × ULN or baseline and bilirubin ≤1.5 × ULN or baseline. Restart at a daily dose 50 mg below the last given dose. Permanently discontinue for recurrent ALT/AST elevations >5 × ULN
Other Non-Hematologic Toxicities	Grade 3 or higher	Interrupt treatment until toxicity resolves to Grade 1 or baseline. Restart at a daily dose 50 mg below the last given dose

Abbreviations: ALT = alanine transaminase; ANC = absolute neutrophil count; AST = aspartate transaminase; CTCAE = Common Terminology Criteria for Adverse Events; ULN = upper limit of normal.

   - Discontinue momelotinib in patients unable to tolerate 100 mg once daily.

5. **Treatment interruption/discontinuation**[1]
   - Myelofibrosis signs and symptoms may flare following interruption or discontinuation of momelotinib.
   - When interrupting or discontinuing momelotinib for reasons other than potentially life-threatening toxicity, consider gradual tapering rather than abrupt discontinuation.

- If signs or symptoms occur, evaluate and treat any intercurrent illness and consider restarting momelotinib.

6. **Drug Interactions**[1]
   - OATP1B1/B3 inhibitors: Concomitant use may increase momelotinib exposure. Monitor for adverse reactions and consider dose modification as clinically indicated.
   - BCRP substrates: Momelotinib may increase exposure of BCRP substrates. For rosuvastatin, initiate at 5 mg once daily and do not exceed 10 mg once daily; follow product-specific recommendations for other BCRP substrates as appropriate.

7. **Monitoring and Toxicity Management**

Monitoring Parameter	Frequency
CBC, including platelet and neutrophil counts	Periodically during treatment and as clinically indicated[1]
Liver tests	Monthly for the first 6 months, then periodically as clinically indicated[1]
Infection	Monitor throughout treatment and treat promptly[1]
HBV reactivation	In patients with chronic HBV infection, treat and monitor according to clinical HBV guidelines.[1]
Constitutional symptoms, spleen-related symptoms, hemoglobin, and transfusion requirements	Assess periodically to evaluate clinical response and transfusion burden.*

*Practice-based consideration

Additional Monitoring/Evaluation:
- Monitor for SCARs, MACE, and development of secondary malignancies.1
- Evaluate patients with signs or symptoms of thrombosis and treat appropriately.1
- Monitor for new or worsening paresthesia (practice-based consideration).

Patient-Centered Activities:
- Patient education
  - Instruct patients to promptly report fever or other signs/symptoms of infection, unusual bleeding or bruising, severe or persistent diarrhea, new or worsening paresthesia, and new or worsening skin changes or rash.
  - Reinforce daily adherence and missed-dose instructions.
  - Advise patients not to interrupt or discontinue momelotinib without discussing with the HCP, as MF signs and symptoms may flare following interruption or discontinuation.
- Medication access:
  - Payer considerations: NCCN lists momelotinib as Preferred, Category 1 for MF-associated anemia with ongoing symptomatic splenomegaly and/or constitutional symptoms; recommendations vary by clinical scenario.[3]
  - Limited distribution: Momelotinib is distributed through an Oncology Optimized Limited Distribution (OOLD) network and may require specialty pharmacy coordination and financial assistance support.

References:

1. OJJAARA® (momelotinib) [prescribing information]. Research Triangle Park, NC: GlaxoSmithKline; 2026.
2. Mesa RA, Kiladjian JJ, Catalano JV, et al. Momelotinib versus danazol in symptomatic, anaemic patients with myelofibrosis previously treated with a JAK inhibitor (MOMENTUM): an international, double-blind, randomised, controlled, phase 3 trial. Lancet. 2023;401(10373):269-280.
3. National Comprehensive Cancer Network. *NCCN Clinical Practice Guidelines in Oncology: Myeloproliferative Neoplasms.* Version 2.2026. National Comprehensive Cancer Network; 2026.