

Revumenib (Revuforj) for the Management of Acute Leukemia

Description:

- This PQI aims to provide information on the administration, management of adverse events, and recommended dose reductions for revumenib.

Background:

- Revumenib is a menin inhibitor and blocks the interaction of both wild-type lysine methyltransferase 2A (KMT2A) and KMT2A fusion proteins with menin. The binding of KMT2A fusion proteins with menin is involved in KMT2A-rearranged (KMT2Ar) acute leukemias through activation of a leukemogenic transcriptional pathway.¹
 - Indicated for adult and pediatric patients with relapsed or refractory acute leukemia who harbor a lysine methyltransferase 2A (KMT2A) translocation.¹
- Adverse reactions reported in $\geq 20\%$ (any grade; excluding lab abnormalities):
 - Hemorrhage
 - Thrombosis
 - Nausea
 - Diarrhea
 - Constipation
 - Musculoskeletal pain
 - Infections
 - Febrile neutropenia
 - Leukocytosis
 - Differentiation syndrome
 - QTc prolongation
 - Decreased appetite
 - Edema
 - Fatigue

PQI Process: Highlights to consider when prescribing and/or processing a prescription for revumenib:

- Confirm indication is appropriate: Revumenib is not currently approved for NPM1(+) disease.
- Verify dosing/administration instructions: Starting dose is 270 mg orally twice daily.

Patient Weight	Without Strong CYP3A4 Inhibitors	With Strong CYP3A4 Inhibitors
40 kg or more	270 mg orally twice daily	160 mg orally twice daily
Less than 40 kg	160 mg/m ² orally twice daily	95 mg/m ² orally twice daily

- For patients weighing less than 40 kg, please refer to package insert for BSA-specific dosing.
- Revumenib should be administered on an empty stomach or with a low-fat meal. Missed doses can be taken up to 12 hours prior to next scheduled dose.
- Assess labs and test results: Revumenib should not be initiated until WBC is less than 25,000/mm³ and QTcF is <450msec.
 - There are no recommended dose adjustments for patients with mild to moderate renal or hepatic impairment.
- Address warnings and precautions:
 - QTc prolongation – Monitor electrocardiograms and electrolytes. Correct hypokalemia and hypomagnesemia prior to and during treatment (Goal K>4 mEq/L, Mg>2 mg/dL).

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- Embryo-fetal toxicity – Can cause fetal harm. Advise patients of risk and use of effective contraception.
- Differentiation syndrome (DS) – Can be potentially fatal or life-threatening. Immediately initiate corticosteroid therapy upon first suspicion. Monitor for signs and symptoms potentially related to DS (fever, dyspnea, hypoxia, pleural/pericardial effusions, peripheral edema, hypotension, renal dysfunction, rapid weight gain, etc.).
- Review drug-drug interactions (based on clinical studies):
 - Revumenib is a major CYP3A4 substrate. Adjust revumenib dose in the presence of strong CYP3A4 inhibitors. Avoid revumenib with concomitant strong or moderate CYP3A4 inducers.
 - Avoid concomitant use of revumenib in combination with QTc prolonging medications. If not possible, obtain ECGs when initiating, during concomitant use, and as clinically indicated.
- Consider supportive care:
 - Patients with acute leukemia are often at risk for infection. Consider the addition of infection prophylaxis, per your institution, and adjust revumenib for any drug interactions including any strong CYP3A4 inhibitors.
- Workup and Monitoring:
 - Presence of KMT2A translocation via peripheral and/or bone marrow evaluation and testing.
 - Obtain blood counts and chemistries prior to initiation and at least monthly to follow.
 - Confirm negative pregnancy status within 7 days prior to treatment initiation in patients of childbearing potential.
 - Complete electrocardiogram assessments prior to treatment initiation and at least once weekly during the first 4 weeks, then at least monthly thereafter. More frequent monitoring may be necessary such as for patients with nausea/vomiting, electrolyte abnormalities, those receiving loop diuretics, or those on concurrent QTc prolonging agents.
 - Track signs/symptoms of DS.

Patient-Centered Activities:

- Advise patients on the risk of developing DS during treatment. It is important for patients to report any signs or symptoms including fever, cough, shortness of breath, low blood pressure, rash, rapid weight gain, swelling or decreased urinary output.
- Advise patients to report any signs or symptoms of feeling faint or loss of consciousness. Inform patients that electrocardiograms may be done periodically to assess heart rhythm while on therapy.
- Advise patients to swallow tablets whole and not to cut or chew tablets. If patients are unable to swallow tablets, they may be crushed and dispersed in water and taken within 2 hours of preparation.
- Instruct patients to inform their health care provider of all new medications to assess for drug-drug interactions.

References:

1. [Revuforj™ \(revumenib\) \[package insert\]](#)
2. Revumenib. Lexicomp Drug Reference - UpToDate. Updated August 2025. Accessed June 2025.
3. National Comprehensive Cancer Network. Acute Myeloid Leukemia (Version 2.2025).

4. National Comprehensive Cancer Network. Acute Lymphoblastic Leukemia (Version 2.2025).
5. Nadiminti KVG., Sahasrabudhe, K.D., Liu, H. Menin inhibitors for the treatment of acute myeloid leukemia: challenges and opportunities ahead. *J Hematol Oncol.* 2024;17(113). doi: 10.1186/s13045-024-01632-8.
6. Candoni A, Coppola G. A 2024 Update on Menin Inhibitors. A New Class of Target Agents against KMT2A-Rearranged and NPM1-Mutated Acute Myeloid Leukemia. *Hematol Rep.* 2024;16(2):244-254. doi: 10.3390/hematolrep16020024.

Supplemental Information:

Revumenib Dosage Modifications for Select Adverse Reactions per package insert¹⁻²:

Adverse Reaction	Recommended Management and Dosing Instructions
Differentiation syndrome	<ul style="list-style-type: none"> - When differentiation syndrome is first suspected, begin hemodynamic monitoring, and administer systemic corticosteroids and continue for a minimum of 3 days and until resolution of symptoms. - Hold revumenib for severe signs/symptoms of DS that persist more than 48 hours after initiation of steroids or immediately for life-threatening symptoms, such as pulmonary symptoms requiring ventilator support. Resume revumenib at the same dose when signs/symptoms improve to grade 1 or lower.
Grade 4 neutropenia or thrombocytopenia	<ul style="list-style-type: none"> - Hold revumenib until recovery to Grade ≤ 2 or baseline and resume at same dose level. If grade 4 neutropenia/thrombocytopenia recurs, hold revumenib until recovery to Grade ≤ 3, then resume revumenib at reduced dose level.
QTc prolongation, corrected using Fridericia's Formula	
QTcF > 480msec to < 500msec	<ul style="list-style-type: none"> - Interrupt revumenib and correct any hypokalemia or hypomagnesemia that may exist. - Resume revumenib at same dose level once QTcF ≤ 480 msec.
QTcF ≥ 500 msec or an increase by >60 msec from baseline	<ul style="list-style-type: none"> - Interrupt revumenib and correct any hypokalemia or hypomagnesemia that may exist. - Resume revumenib at reduced dose level once QTcF ≤ 480 msec.
QTcF prolongation associated with life-threatening arrhythmias	<ul style="list-style-type: none"> - Permanently discontinue.
Electrolyte abnormalities	
Potassium (K) 3.6-3.9 mEq/L and/or Magnesium (Mg) 1.7-1.9 mg/dL	Supplement potassium and/or magnesium and continue revumenib
Potassium ≤ 3.5 mEq/L and/or Magnesium ≤ 1.6 mg/dL	Supplement potassium and/or magnesium and recheck electrolytes within 24 hours Repeat within 24 hours: <ul style="list-style-type: none"> - Potassium >3.5 mEq/L and/or magnesium >1.6 mg/dL: continue revumenib - Potassium ≤ 3.5 mEq/L and/or magnesium ≤ 1.6 mg/dL: Hold revumenib and continue supplementation. Resume revumenib at same dose once electrolytes reach adequate levels (K >3.5 mEq/L, Mg >1.6 mg/dL)