DOSING & ADMINISTRATION GUIDE

Revuforj®
(revumenib) tablets
25 mg • 110 mg • 160 mg

A first-in-class, oral, selective menin inhibitor specifically designed to target and disrupt the key driver of acute leukemia with a *KMT2A* translocation

INDICATION

Revuforj® (revumenib) is a menin inhibitor indicated for the treatment of relapsed or refractory acute leukemia with a lysine methyltransferase 2A gene (*KMT2A*) translocation in adult and pediatric patients 1 year and older.

IMPORTANT SAFETY INFORMATION

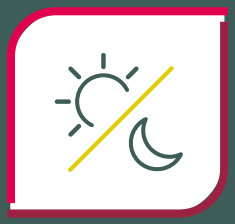
WARNING: DIFFERENTIATION SYNDROME

Differentiation syndrome, which can be fatal, has occurred with Revuforj. Signs and symptoms may include fever, dyspnea, hypoxia, pulmonary infiltrates, pleural or pericardial effusions, rapid weight gain or peripheral edema, hypotension, and renal dysfunction. If differentiation syndrome is suspected, immediately initiate corticosteroid therapy and hemodynamic monitoring until symptom resolution.

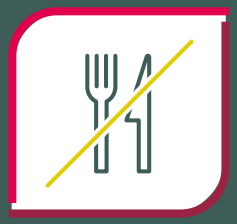
Please see Important Safety Information throughout and Full Prescribing Information, including BOXED WARNING.

Convenience of an oral, targeted treatment

All Revuforj® (revumenib) doses should be taken:



orally, twice daily at about the same time each day (~12 hours apart)



fasted* or with a low-fat meal (~400 calories and ≤25% fat)

Continue Revuforj until disease progression or unacceptable toxicity

*In the clinical trial protocol, fasted was defined as at least 2 hours after a meal and 1 hour before the next meal.

For patients without disease progression or unacceptable toxicity, treat for a minimum of 6 months to allow time for a clinical response

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The recommended dose of Revuforj varies by patient weight and concomitant use of strong CYP3A4 inhibitors

25 mg **110 mg** **160 mg**

Bottles and tablets shown are not actual size.

- If needed, attain the desired dose by combining different strengths of Revuforj tablets
- Advise patients to swallow tablets whole and to not 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

Review the Medication Guide and Instructions for Use with patients and/or their respective caregivers.

Missed dose

If a dose of Revuforj is missed or not taken at the usual time, administer the dose as soon as possible on the same day and at least 12 hours prior to the next scheduled dose. Return to the normal schedule the following day. Do not administer 2 doses within 12 hours

Oral twice-daily dosing

Recommended doses for patients 1 year and older:

Without a strong CYP3A4 inhibitor*

Dose level	Patients ≥40 kg	Patients <40 kg*
Starting dose	270 mg BID	160 mg/m² BID
Reduced dose	160 mg BID	95 mg/m² BID

With a strong CYP3A4 inhibitor†

Dose level	Patients ≥40 kg	Patients <40 kg*
Starting dose	160 mg BID	95 mg/m² BID
Reduced dose	110 mg BID	65 mg/m² BID

***For patients weighing <40 kg with a BSA ≤1.4 m²:**
Please see the table to the right for the recommended dose and the reduced dose

- If needed, attain the desired dose by combining different strengths of Revuforj tablets
- Concurrent use of standard intrathecal chemotherapy prophylaxis is recommended for patients with risk of central nervous system relapse

†If the strong CYP3A4 inhibitor is discontinued, increase the Revuforj dose (after at least 5 half-lives of the strong CYP3A4 inhibitor) to the recommended dosage without strong CYP3A4 inhibitors.

BID=twice a day; BSA=body surface area; CYP3A4=cytochrome P450 3A4.

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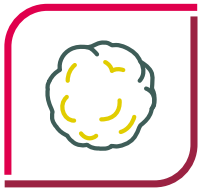
Total tablet dosage by BSA for patients weighing <40 kg based on the recommended starting dose or reduced dose of Revuforj

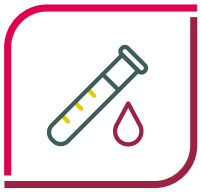
	Revuforj dosage for recommended dose and reduced dose		
BSA (m²)	160 mg/m²	95 mg/m²	65 mg/m²
1.4	220 mg BID	135 mg BID	100 mg BID
1.3	220 mg BID	135 mg BID	75 mg BID
1.2	185 mg BID	110 mg BID	75 mg BID
1.1	185 mg BID	110 mg BID	75 mg BID
1	160 mg BID	100 mg BID	50 mg BID
0.9	135 mg BID	75 mg BID	50 mg BID
0.8	135 mg BID	75 mg BID	50 mg BID
0.7	110 mg BID	50 mg BID	50 mg BID
0.6	100 mg BID	50 mg BID	25 mg BID
0.5	75 mg BID	50 mg BID	25 mg BID
0.4	50 mg BID	25 mg BID	25 mg BID

For patients who are unable to swallow Revuforj tablets whole:
Review the **Instructions for Use** with patients and their caregivers for how to prepare and break apart the Revuforj tablets in water

Monitoring guidance before and during treatment



Reduce the white blood cell count to less than 25 Gi/L prior to the initiation of Revuforj



Assess blood counts, electrolytes, and liver enzymes prior to the initiation of Revuforj and monthly thereafter

Perform electrocardiogram (ECG) prior to the initiation of Revuforj, at least once a week for the first 4 weeks, and at least monthly thereafter

IMPORTANT SAFETY INFORMATION (*cont'd*)

WARNINGS AND PRECAUTIONS

Differentiation syndrome: Revuforj can cause fatal or life-threatening differentiation syndrome (DS). Symptoms of DS, including those seen in patients treated with Revuforj, include fever, dyspnea, hypoxia, peripheral edema, pleuropericardial effusion, acute renal failure, and/or hypotension. In clinical trials, DS occurred in 39 (29%) of 135 patients treated with Revuforj. DS was Grade 3 or 4 in 13% of patients and fatal in one. The median time to onset was 10 days (range 3-41 days). Some patients experienced more than 1 DS event. Treatment interruption was required for 7% of patients, and treatment was withdrawn for 1%.

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Monitor for QTc interval prolongation and manage any abnormalities promptly

- Do not initiate Revuforj in patients with QTcF >450 msec
- Correct electrolyte abnormalities, including hypokalemia and hypomagnesemia, prior to treatment with Revuforj

Verify pregnancy status in females of reproductive potential within 7 days prior to initiating Revuforj

IMPORTANT SAFETY INFORMATION (*cont'd*)

WARNINGS AND PRECAUTIONS (*cont'd*)

Differentiation syndrome (*cont'd*): Reduce the white blood cell count to less than 25 Gi/L prior to starting Revuforj. If DS is suspected, immediately initiate treatment with systemic corticosteroids (e.g., dexamethasone 10-mg IV every 12 hours in adults or dexamethasone 0.25-mg/kg/dose IV every 12 hours in pediatric patients weighing less than 40 kg) for a minimum of 3 days and until resolution of signs and symptoms. Institute supportive measures and hemodynamic monitoring until improvement. Interrupt Revuforj if severe signs and/or symptoms persist for more than 48 hours after initiation of systemic corticosteroids, or earlier if life-threatening symptoms occur such as pulmonary symptoms requiring ventilator support. Restart steroids promptly if DS recurs after tapering corticosteroids.

QTc interval prolongation: In the clinical trials, QTc interval prolongation was reported as an adverse reaction in 39 (29%) of 135 patients treated with Revuforj. QTc interval prolongation was Grade 3 in 12% of patients. The heart-rate corrected QT interval (using Fridericia's method) (QTcF) was greater than 500 msec in 8%, and the increase from baseline QTcF was greater than 60 msec in 18%. Revuforj dose reduction was required for 5% of patients due to QTc interval prolongation. QTc prolongation occurred in 16% of the 31 patients less than 17 years old, 33% of the 88 patients 17 years to less than 65 years old, and in 50% of the 16 patients 65 years or older.

Differentiation syndrome

Differentiation syndrome, which can be fatal, has occurred with Revuforj

In clinical trials, differentiation syndrome occurred in 29% of patients (39/135), including:

- 32% of patients with acute myeloid leukemia (AML)
- 25% of patients with mixed-phenotype acute leukemia (MPAL)
- 14% of patients with acute lymphoblastic leukemia (ALL)

The median time to onset was 10 days (range 3-41 days)

- Differentiation syndrome was Grade 3 or 4 in 13% of patients and fatal in one
- Some patients experienced more than 1 event of differentiation syndrome
- Treatment interruption was required for 7% of patients, and treatment was withdrawn for 1%

Symptoms of differentiation syndrome, including those seen in patients treated with Revuforj, include:

- Fever
- Dyspnea
- Hypoxia
- Peripheral edema
- Pleuropericardial effusion
- Acute renal failure
- Hypotension

Advise patients and their caregivers to contact you or go to the nearest hospital emergency room immediately if the patient develops any symptoms of differentiation syndrome while taking Revuforj

Encourage your patients to download the Differentiation Syndrome Wallet Card at Revuforj.com

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QTc interval prolongation

In the clinical trials, QTc interval prolongation was reported as an adverse reaction in 29% of patients (39/135), including:

- 16% of the 31 patients less than 17 years old
- 33% of the 88 patients 17 years to less than 65 years old
- 50% of the 16 patients 65 years or older

The heart-rate corrected QT interval (using Fridericia's method) (QTcF) was greater than 500 msec in 8%, and the increase from baseline QTcF was greater than 60 msec in 18%.

- QTc interval prolongation was Grade 3 in 12% of patients
- Revuforj dose reduction was required for 5% due to QTc interval prolongation

In patients with congenital long QTc syndrome, congestive heart failure, electrolyte abnormalities, or those who are taking medications known to prolong the QTc interval, more frequent ECG monitoring may be necessary.

Embryo-fetal toxicity

Revuforj can cause fetal harm when administered to a pregnant woman. Advise pregnant women of the potential risk to a fetus.

Advise females of reproductive potential and males with female partners of reproductive potential to use effective contraception during treatment with Revuforj and for 4 months after the last dose of Revuforj.

Verify pregnancy status in females of reproductive potential within 7 days prior to initiating Revuforj.

Other drugs may affect the safety and efficacy of Revuforj

Concomitant use of Revuforj with:	Action
Strong CYP3A4 inhibitors increases revumenib systemic exposure, which may increase the risk of adverse reactions	If concomitant use of strong CYP3A4 inhibitors is required, reduce Revuforj dose*
Strong or moderate CYP3A4 inducers may decrease revumenib and increase M1 systemic exposure, which may reduce Revuforj efficacy or increase the risk of QT prolongation associated with the M1 metabolite	Avoid concomitant use with Revuforj
QTc-prolonging drugs may result in an increase in the QTc interval and adverse reactions associated with QTc interval prolongation	Avoid concomitant use with Revuforj†

*See Section 2.2 of the Full Prescribing Information.
†If concomitant use is unavoidable, obtain ECGs when initiating, during concomitant use, and as clinically indicated. Withhold Revuforj if the QTc interval is >480 msec. Restart Revuforj after the QTc interval returns to ≤480 msec.

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Doses can be modified as needed to help manage adverse reactions

Adverse reaction	Recommended action
Differentiation syndrome	• If differentiation syndrome is suspected, administer systemic corticosteroids and initiate hemodynamic monitoring until symptom resolution and for a minimum of 3 days • Interrupt Revuforj if severe signs and/or symptoms persist for more than 48 hours after initiation of systemic corticosteroids, or earlier for life-threatening symptoms such as pulmonary symptoms requiring ventilator support. Resume Revuforj at the same dose when signs and symptoms improve to Grade 1‡ or lower
Noninfectious leukocytosis	• Initiate treatment with hydroxyurea in patients with an elevated or rapidly rising leukocyte count. Add leukapheresis if clinically indicated • Taper hydroxyurea only after leukocytosis improves or resolves
QTc interval greater than 480 msec to 500 msec	• Interrupt Revuforj • Check electrolyte levels. Correct hypokalemia and hypomagnesemia • Restart Revuforj at the same dose level after the QTc interval returns to less than or equal to 480 msec

Other actions may be necessary based on your clinical judgment.

‡Grade 1 is mild, Grade 2 is moderate, Grade 3 is severe, Grade 4 is life-threatening. Severity as defined by National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE version 5.0).

Dose modifications (*cont'd*)

Adverse reaction	Recommended action
QTc interval greater than 500 msec (Grade 3*)	• Interrupt Revuforj • Check electrolyte levels. Correct hypokalemia and hypomagnesemia • Restart Revuforj at the reduced dose level† after the QTc interval returns to less than or equal to 480 msec
Potassium 3.6-3.9 mEq/L, and/or Magnesium 1.7-1.9 mg/dL or 0.66-0.81 mmol/L	• Supplement potassium and/or magnesium • Continue Revuforj
Potassium ≤3.5 mEq/L, and/or Magnesium ≤1.6 mg/dL or 0.65 mmol/L	• Supplement potassium and/or magnesium, and recheck levels within 24 hours • On recheck of potassium and magnesium labs within 24 hours, if potassium is greater than 3.5 mEq/L and/or magnesium is greater than 1.6 mg/dL, continue Revuforj. If potassium is less than 3.5 mEq/L and/or magnesium is less than 1.6 mg/dL, hold Revuforj and continue supplementation; resume Revuforj at the same dose level when the correction is complete

Other actions may be necessary based on your clinical judgment.

Adverse reaction	Recommended action
QTc interval prolongation with signs/symptoms of life-threatening arrhythmia, Torsades de pointes, polymorphic ventricular tachycardia, signs/symptoms of life-threatening arrhythmia (Grade 4*); Grade 3* or higher allergic reactions	• Permanently discontinue Revuforj
Other nonhematological adverse reactions Grade ≥3*	• Interrupt Revuforj until recovery to Grade 1* or baseline • If recovered in ≤7 days, restart Revuforj at the same dose level. If the same Grade ≥3* toxicity recurs, interrupt Revuforj until recovery to Grade 1* or baseline. Restart Revuforj at the reduced dose level† • If recovered in >7 days, restart Revuforj at the reduced dose level† If the same Grade ≥3* toxicity recurs, discontinue Revuforj
Grade 4* neutropenia or thrombocytopenia	• Interrupt Revuforj until recovery to Grade ≤2* or baseline • Restart Revuforj at the same dose level • If Grade 4* neutropenia or thrombocytopenia recurs without attributable cause, interrupt Revuforj until recovery to Grade ≤3.* Restart Revuforj at the reduced dose level†

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†See Tables 4, 5, and 6 in the Full Prescribing Information for the reduced dose levels.

IMPORTANT SAFETY INFORMATION (*cont'd*)

WARNINGS AND PRECAUTIONS (*cont'd*)

QTc interval prolongation (*cont'd*): Correct electrolyte abnormalities, including hypokalemia and hypomagnesemia, prior to treatment with Revuforj. Perform an electrocardiogram (ECG) prior to initiation of Revuforj, and do not initiate Revuforj in patients with QTcF >450 msec. Perform an ECG at least once weekly for the first 4 weeks and at least monthly thereafter. In patients with congenital long QTc syndrome, congestive heart failure, electrolyte abnormalities, or those who are taking medications known to prolong the QTc interval, more frequent ECG monitoring may be necessary. Concomitant use with drugs known to prolong the QTc interval may increase the risk of QTc interval prolongation.

- Interrupt Revuforj if QTcF increases >480 msec and <500 msec, and restart Revuforj at the same dose twice daily after the QTcF interval returns to ≤480 msec
- Interrupt Revuforj if QTcF increases >500 msec or by >60 msec from baseline, and restart Revuforj twice daily at the lower-dose level after the QTcF interval returns to ≤480 msec
- Permanently discontinue Revuforj in patients with ventricular arrhythmias and in those who develop QTc interval prolongation with signs or symptoms of life-threatening arrhythmia

Embryo-fetal toxicity: Revuforj can cause fetal harm when administered to a pregnant woman. Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential and males with female partners of reproductive potential to use effective contraception during treatment with Revuforj and for 4 months after the last dose of Revuforj.

ADVERSE REACTIONS

Fatal adverse reactions occurred in 4 (3%) patients who received Revuforj, including 2 with differentiation syndrome, 1 with hemorrhage, and 1 with sudden death.

Serious adverse reactions were reported in 99 (73%) patients. The most frequent **serious adverse reactions** (≥5%) were infection (24%), febrile neutropenia (19%), bacterial infection (17%), differentiation syndrome (12%), hemorrhage (9%), and thrombosis (5%).

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IMPORTANT SAFETY INFORMATION (*cont'd*)

ADVERSE REACTIONS (*cont'd*)

The most **common adverse reactions** (≥20%) including laboratory abnormalities, were hemorrhage (53%), nausea (51%), phosphate increased (50%), musculoskeletal pain (42%), infection (41%), aspartate aminotransferase increased (37%), febrile neutropenia (35%), alanine aminotransferase increased (33%), parathyroid hormone intact increased (33%), bacterial infection (31%), diarrhea (30%), differentiation syndrome (29%), electrocardiogram QT prolonged (29%), phosphate decreased (25%), triglycerides increased (25%), potassium decreased (24%), decreased appetite (24%), constipation (23%), edema (23%), viral infection (23%), fatigue (22%), and alkaline phosphatase increased (21%).

DRUG INTERACTIONS

Drug interactions can occur when Revuforj is concomitantly used with:

- Strong CYP3A4 inhibitors: reduce Revuforj dose
- Strong or moderate CYP3A4 inducers: avoid concomitant use with Revuforj
- QTc-prolonging drugs: avoid concomitant use with Revuforj. If concomitant use is unavoidable, obtain ECGs when initiating, during concomitant use, and as clinically indicated. Withhold Revuforj if the QTc interval is >480 msec. Restart Revuforj after the QTc interval returns to ≤480 msec

SPECIFIC POPULATIONS

Lactation: advise lactating women not to breastfeed during treatment with Revuforj and for 1 week after the last dose.

Pregnancy and testing: Revuforj can cause fetal harm when administered to a pregnant woman. Verify pregnancy status in females of reproductive potential within 7 days prior to initiating Revuforj.

Pediatric: monitor bone growth and development in pediatric patients.

Geriatric: compared to younger patients, the incidences of QTc prolongation and edema were higher in patients 65 years and older.

Infertility: based on findings in animals, Revuforj may impair fertility. The effects on fertility were reversible.

To report SUSPECTED ADVERSE REACTIONS, contact Syndax Pharmaceuticals at 1-888-539-3REV or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

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Learn more about Revuforj and how to get your patients started on treatment at

Revuforjhcp.com

CLICK TO WATCH NOW

Encourage patients and/or their respective caregivers to watch the Instructions for Use video for step-by-step guidance on how to prepare and administer Revuforj to people who are unable to swallow tablets whole

The content provided here is for informational purposes only and is not a substitute for your medical judgment.

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Reference: Revuforj® [Prescribing Information]. Syndax Pharmaceuticals Inc.; November 2024.

Syndax