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

A CLINICAL GUIDE FOR HEALTHCARE PROFESSIONALS AS YOU HELP YOUR PATIENTS

FORJ FORWARD

INDICATION

Revuforj 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.

Understanding how Revuforj works

The first-in-class, oral menin inhibitor

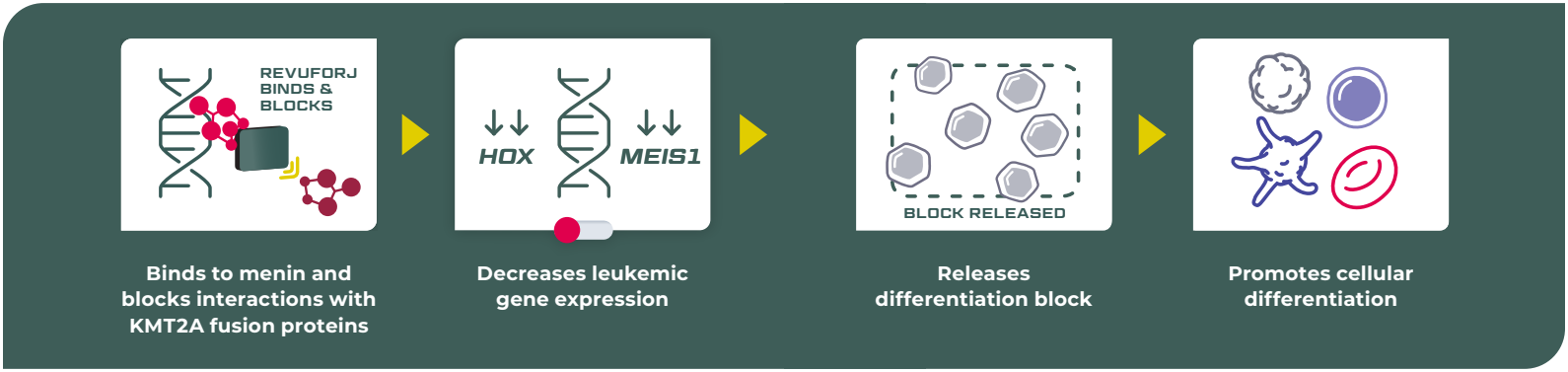
Revuforj is the only targeted therapy approved for use in adult and pediatric patients 1 year and older who have any lineage of relapsed or refractory acute leukemia with a *KMT2A* translocation.[1]

Revuforj works differently

Revuforj selectively targets and inhibits menin-KMT2A protein interactions—the key driver of acute leukemia with a *KMT2A* rearrangement, including translocations.[1,2]

~95% of patients with *KMT2Ar* acute leukemia have a *KMT2A* translocation[3]

A *KMT2A* translocation is a type of *KMT2A* rearrangement (*KMT2Ar*) that occurs when part of one chromosome breaks and fuses to a different chromosome



HOX=homeobox; KMT2A=lysine methyltransferase 2A; *MEIS1*=*MEIS* homeobox-1.

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%.

IMPORTANT SAFETY INFORMATION (*cont'd*)

WARNINGS AND PRECAUTIONS

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.

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Differentiation syndrome

Differentiation syndrome, which can be fatal, has occurred with Revuforj[1]

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[1]:

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

Advise patients and their caregivers to call their healthcare team or go to the nearest hospital emergency room immediately if the patient develops any of these symptoms while taking Revuforj.

Reduce the white blood cell count to less than 25 Gi/L prior to starting Revuforj[1]

If differentiation syndrome is suspected, immediately initiate treatment with systemic corticosteroids for a **minimum of 3 days** and until resolution of signs and symptoms.

Treatment example:

Patients ≥40 kg:
dexamethasone
10-mg IV every 12 hours

Patients <40 kg:
dexamethasone
0.25-mg/kg/dose IV every 12 hours

IMPORTANT SAFETY INFORMATION (*cont'd*)

WARNINGS AND PRECAUTIONS

Differentiation syndrome (*cont'd*): 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.

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Monitoring guidance

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

Monitor for QTc interval prolongation and manage any abnormalities promptly[1]

- 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

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.

IMPORTANT SAFETY INFORMATION (*cont'd*)

WARNINGS AND PRECAUTIONS

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.

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Dosage form & administration

Convenience of an oral, targeted treatment[1]

All Revuforj doses should be taken:

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

on an empty stomach
at least 2 hours after a meal and 1 hour before the next meal*

*As defined by the clinical trial protocol.

OR

with a low-fat meal
low-fat meals should be about 400 calories and contain 25% or less fat

Continue Revuforj until disease progression or unacceptable toxicity

>6 MONTHS

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

The recommended dose of Revuforj varies by patient weight and concomitant use of strong CYP3A4 inhibitors[1]

Bottles and tablets shown are not actual size.

25 mg | 110 mg | 160 mg

- 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. **See Instructions for Use**

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.

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Oral twice-daily dosing

Recommended doses for patients 1 year and older[1]:

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 Section 2.2, Table 2 and Section 2.3, Table 6 of the **Full Prescribing Information** 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.

Prior to the initiation of Revuforj[1]:

Reduce the white blood cell count to less than 25 Gi/L

Assess blood counts, electrolytes, and liver enzymes

Perform an electrocardiogram (ECG)

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

IMPORTANT SAFETY INFORMATION (*cont'd*)

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

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Adverse reactions

The safety of Revuforj reflects exposure in 135 patients (104 adult and 31 pediatric) with relapsed or refractory acute leukemia with a *KMT2A* translocation[1]

Adverse reactions reported in ≥20% (any Grade) or ≥5% (Grade 3 or 4)

Adverse reaction	All Grades (%)	Grade 3 or 4 (%)
Vascular disorders		
Hemorrhage*†	53	9
Thrombosis†	10	5
Gastrointestinal disorders		
Nausea†	51	4
Diarrhea†	30	4
Constipation	23	1
Musculoskeletal and connective tissue disorders		
Musculoskeletal pain†	42	6
Infections and infestations		
Infection†	41	29
Bacterial infection†	31	20
Viral infection†	23	4
Blood and lymphatic system disorders		
Febrile neutropenia	35	33
Leukocytosis	8	5
Neoplasms benign, malignant, and unspecified (including cysts and polyps)		
Differentiation syndrome*	29	13
Investigations		
Electrocardiogram QT prolonged	29	12
Metabolism and nutrition disorders		
Decreased appetite	24	8
General disorders and administration site conditions		
Edema†	23	1
Fatigue†	22	5

*Includes the following fatal adverse reactions: differentiation syndrome (n=2); hemorrhage (n=1).

†These represent grouped terms for adverse reactions. Please see Table 7 in the **Full Prescribing Information** for complete definitions of grouped terms.

IMPORTANT SAFETY INFORMATION (*cont'd*)

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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Drug interactions

Other drugs may affect the safety and efficacy of Revuforj[1]

Ask patients to tell you or their healthcare provider about any other medications they are taking, including prescription and over-the-counter medicines, vitamins, and herbal supplements. Remind patients that taking Revuforj with other medicines may affect each other, causing side effects.

Concomitant use of Revuforj with:	Action
Strong CYP3A4 inhibitors	Reduce Revuforj dose*
Strong or moderate CYP3A4 inducers	Avoid concomitant use with Revuforj
QTc-prolonging drugs	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.

IMPORTANT SAFETY INFORMATION (*cont'd*)

ADVERSE REACTIONS

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%).

Laboratory abnormalities

Selected new or worsening laboratory abnormalities in patients with R/R acute leukemia with a *KMT2A* translocation[1]

Laboratory abnormality	Grades 1-4‡ (%)	Grade 3-4 (%)
Phosphate increased	50	–
Aspartate aminotransferase increased	37	1
Alanine aminotransferase increased	33	3
Parathyroid hormone, intact increased	33	–
Phosphate decreased	25	–
Triglycerides increased	25	3
Potassium decreased	24	5
Alkaline phosphatase increased	21	0
Cholesterol increased	19	0
Creatinine increased	19	0
Calcium corrected increased	15	0

‡The denominator used to calculate the rate varied from 73 to 135 based on the number of patients with a baseline value and at least 1 post-baseline value.

CYP3A4=cytochrome P450 3A4; ECG=electrocardiogram; *KMT2A*=lysine methyltransferase 2A; R/R=relapsed/refractory.

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Dose modifications

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
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.

*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).

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

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

Dose modifications (*cont'd*)

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†

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).

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

Forj forward

Tips that may help your patients while on Revuforj

- Advise patients and caregivers to read the FDA-approved **Medication Guide and Instructions for Use**
- Inform patients and caregivers that serious adverse reactions may occur with Revuforj, including differentiation syndrome and QTc prolongation
- Advise patients to inform their healthcare provider if they are pregnant or plan to become pregnant as Revuforj can harm their unborn baby
- Educate patients and caregivers on the symptoms of differentiation syndrome and QTc prolongation, as well as the importance of reporting any suspected adverse reaction early and often. Remind patients to carry the **Differentiation Syndrome Wallet Card** at all times
- Encourage patients and caregivers to contact their healthcare team or go to the nearest hospital emergency room if they develop any symptoms of differentiation syndrome
- Advise patients to inform their healthcare provider of all concomitant products, including over-the-counter products and supplements
- Remind patients that a dose modification or dose delay in treatment is acceptable due to an adverse reaction. Patients who experience severe reactions may need to permanently discontinue treatment

SyndAccess™

Learn more about the SyndAccess™ Patient Support Program and what's available to support your patients

SyndAccess.com/hcp
1-888-567-SYND (7963)
Monday–Friday, 9 AM–6 PM ET

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GET MORE INFORMATION AT
Revuforjhcp.com

IMPORTANT SAFETY INFORMATION (*cont'd*)

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.

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

References: 1. Revuforj. [Prescribing Information]. Waltham, MA: Syndax Pharmaceuticals Inc.; November 2024. **2.** Issa GC, et al. *Leukemia*. 2021;35:2482-2495. **3.** Meyer C, et al. *Leukemia*. 2023;37:988-1005.

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