revumenib (Revuforj®)

EOCCO POLICY

Policy Type:PA/SP Pharmacy Coverage Policy: EOCCO324

Description

Revumenib (Revuforj) is an orally administered menin inhibitor for the treatment of relapsed or refractory acute leukemia with a lysine methyltransferase 2A (KMT2A) gene translocation.

Length of Authorization

- Initial: Six months
- Renewal: 12 months

Quantity Limits

Product Name	Indication	Dosage Form	Quantity Limit
revumenib (Revuforj)	Acute myeloid leukemia, relapsed/refractory Acute lymphoblastic leukemia, relapsed/refractory	25 mg tablets	60 capsules/30 days
		110 mg tablets	
		160 mg tablets	

Initial Evaluation

I. **Revumenib (Revuforj)** may be considered medically necessary when the following criteria are met:
   A. Member is one year of age or older; **AND**
   B. A documented height and weight or BSA within the last 3 months; **AND**
   C. Medication is prescribed by, or in consultation with, an oncologist or hematologist; **AND**
   D. Medication will not be used in combination with any other oncology therapy; **AND**
   E. Attestation that the member does not qualify for any actively enrolling clinical trials for the treatment of AML or ALL; **AND**
   F. A diagnosis of **relapsed or refractory acute leukemia [i.e., acute myeloid leukemia (AML) or acute lymphocytic leukemia (ALL)]** when all the following are met:
      1. Presence of KMT2A mutation status as detected by an FDA-approved test; **AND**
      2. Treatment with one of the following has been ineffective, or not tolerated unless both are contraindicated:
         i. Systemic chemotherapy; **OR**
         ii. Allogenic hematopoietic stem cell transplant; **AND**
      3. Provider attestation that all standard therapies have been exhausted.

II. Revumenib (Revuforj) is considered investigational when used for all other conditions, including but not limited to:

A. Revumenib (Revuforj) used in combination with another oncology therapy
B. Newly diagnosed acute leukemia
C. Acute leukemia in the absence of KMT2A mutation
D. Acute leukemia with an NPM1 mutation

Renewal Evaluation

I. Member has received a previous prior authorization approval for this agent through this health plan or has been established on therapy from a previous health plan; **AND**
II. Member is not continuing therapy based off being established on therapy through samples, manufacturer coupons, or otherwise. If they have, initial policy criteria must be met for the member to qualify for renewal evaluation through this health plan; **AND**
III. Medication will not be used in combination with any other oncology therapy; **AND**
IV. Member has exhibited improvement or stability of disease symptoms [e.g., no signs of unacceptable toxicity or intolerance, no signs of disease progression, become independent of red blood cell and platelet transfusion]

Supporting Evidence

I. Given the complexities involved with the diagnosis and management of acute myeloid leukemia (AML) and acute lymphoblastic leukemia (ALL), treatment with revumenib (Revuforj) must be initiated and/or supervised by an oncologist or hematologist. Choice of initial and later-line therapies in the setting of relapsed/refractory (R/R) AML and ALL are contingent upon patient specific characteristics, disease-risk, and cytogenetic stratification.
II. Revumenib (Revuforj) is a menin inhibitor that was studied in an open-label, single-arm, multicenter Phase I/II trial of 135 participants with relapsed/refractory AML or ALL with a confirmed KMT2A gene rearrangement mutation (AUGMENT-101). Participants included children and adults with a median age of 35 years, female (64%), highly refractory relapsed patients who had at least one relapse with no response to their most recent salvage therapy (59%). For inclusion participants must have tried at least one previous line of therapy. Participants received a twice daily dose of revumenib (Revuforj) and the efficacy measure was the rate of complete remission (CR) or CR with partial hematological recovery (CRh), duration of CR+CRh, and the conversion from transfusion dependence to independence. The efficacy analysis included 104 participants and 21.2% achieved CR+CRh, a median duration of response of 6.4 months, and 14% of transfusion dependent participants became independent while 48% of independent participants remained transfusion independent.
III. Common adverse reactions include hemorrhage (53%), nausea (51%), musculoskeletal pain (42%), infection (41%), and febrile neutropenia (35%) on revumenib (Revuforj) treatment. Serious adverse reactions were reported in 73% of participants which included infection (24%),

febrile neutropenia (19%), bacterial infection (17%), differentiation syndrome (12%), hemorrhage (9%), and thrombosis (5%).

IV. There were 14 documented deaths at the interim analysis cutoff during the Phase II review, in which five individual participants who experienced an intracranial hemorrhage, myocardial ischemia, pneumonia, and respiratory failure were deemed to be possibly related to revumenib (Revuforj).

V. National Comprehensive Cancer Network (NCCN) guidelines for the treatment of AML were updated in January 2025 to recommend revumenib (Revuforj) as monotherapy for relapsed/refractory disease with KMT2A mutation as category 2A recommendation. This is then suggested to be followed by hematopoietic stem cell transplantation (HSCT). Other therapies include intensive and less intensive chemotherapy regimens based on patient-specific factors and tolerability, which most are listed as a 2A recommendation except for CLIA + venetoclax and LDAC, which are category 2B.

VI. National Comprehensive Cancer Network (NCCN) guidelines for the treatment of ALL were updated in December 2024 to recommend revumenib (Revuforj) as monotherapy for relapsed/refractory disease with a KMT2A mutation as a category 2A recommendation. This recommendation is for disease with Philadelphia (Ph) positive - B-ALL and T-ALL; the recommendation is not included in Ph+ B-ALL disease. Other treatments for Ph- B-ALL include blinatumomab (Blincyto) and inotuzumab (Besponsa), which are listed as a category 1 recommendation. Additional therapies in this space also include CAR T-cell therapies. Other treatments for T-ALL prefers nelarabine with or without etoposide and cyclosporine, along with other chemotherapy combinations including venetoclax, bortezomib, cytarabine or fludarabine-containing regimens.

Investigational or Not Medically Necessary Uses

I. Revumenib (Revuforj) has not been FDA-approved, or sufficiently studied for safety and efficacy for the conditions or settings listed below:
   - A. Use in combination therapy with other oncolytic agents
     - i. Current clinical trial data leading to FDA approval is in the monotherapy setting. Safety and efficacy has not been established for combination regimens.
   - B. Treatment of newly diagnosed acute leukemia
     - i. There is no published data to support use of revumenib (Revuforj) in newly diagnosed patients.
     - ii. Clinical trials are being conducted in patients with newly diagnosed AML. There is currently insufficient evidence to support the safety and efficacy of revumenib (Revuforj) for the treatment of newly diagnosed disease.
   - C. Treatment of acute leukemia without a known KMT2Ar mutation

i. There is lack of evidence to suggest the use of revumenib (Revuforj) in patients with acute leukemia without a KMT2Ar mutation. Patients who did not have confirmed mutation status were excluded from the trials.

D. Treatment of acute leukemia with an NPM1 mutation
   i. This is part of the ongoing phase 2C of the AUGMENT-101 trial for use in relapsed/refractory AML with an NPM1 mutation. As of March 2025, data to support use in this population has not been published.

References

1. Revuforj product dossier. Syndax Pharmaceuticals, Inc; January 2025.
2. Revuforj. Package Insert. Syndax Pharmaceuticals, Inc; November 2024.
3. NCCN Clinical Practice Guidelines in Oncology. Acute Lymphoblastic Leukemia. Version 3.2024. Accessed March 11, 2025. https://www.nccn.org/professionals/physician_gls/pdf/all.pdf
4. NCCN Clinical Practice Guidelines in Oncology. Acute Myeloid Leukemia. Version 2.2025. Accessed March 11, 2025. https://www.nccn.org/professionals/physician_gls/pdf/aml.pdf
5. Issa GC, Aldoss I, Thirman MJ, et al. Menin Inhibition With Revumenib for KMT2A-Rearranged Relapsed or Refractory Acute Leukemia (AUGMENT-101). J Clin Oncol. 2025;43(1):75-84. doi:10.1200/JCO.24.00826

Related Policies

Policies listed below may be related to the current policy. Related policies are identified based on similar indications, similar mechanisms of action, and/or if a drug in this policy is also referenced in the related policy

Policy Name	Disease state
venetoclax (Venclexta®)	Newly diagnosed acute myeloid leukemia (AML)
azacitidine (Onureg®)	Acute Myeloid Leukemia (AML), maintenance treatment after first complete remission
glasdegib (DAURISMO®)	Newly diagnosed acute myeloid leukemia (AML)
midostaurin (Rydapt®)	Acute myeloid leukemia, newly diagnosed, FLT3 mutation-positive, in combination with cytarabine/daunorubicin induction and cytarabine consolidation
dasatinib (SPRYCEL®)	Philadelphia chromosome-positive (Ph+) acute myeloid leukemia (ALL)
ponatinib (Iclusig ®)	Newly diagnosed Ph+ ALL in combination with chemotherapy
IDH Inhibitors	Acute myeloid leukemia, relapsed/refractory; Acutely myeloid leukemia, newly diagnosed
gilteritinib (XOSPATA®)	Relapsed/refractory FLT3-mutated acute myeloid leukemia (AML)
imatinib (Gleevec®)	Philadelphia chromosome-positive acute lymphoblastic leukemia, newly diagnosed, in combination with chemotherapy Philadelphia chromosome-positive acute lymphoblastic leukemia, relapsed/refractory

Policy Implementation/Update:

Action and Summary of Changes	Date
Policy created	05/2025