Pharmacy Policy Bulletin: J-1429 Revuforj (revumenib) – Commercial and Healthcare Reform	
Number: J-1429	**Category:** Prior Authorization
Line(s) of Business: ☒ Commercial ☒ Healthcare Reform ☐ Medicare	**Benefit(s):** **Commercial:** **Prior Authorization (1.):** **1.** Miscellaneous Specialty Drugs Oral = Yes w/ Prior Authorization **Healthcare Reform:** Not Applicable
Region(s): ☒ All ☐ Delaware ☐ New York ☐ Pennsylvania ☐ West Virginia	**Additional Restriction(s):** None
Version: J-1429-002	**Original Date: 01/29/2025**
Effective Date: 04/25/2025	**Review Date: 04/09/2025**

Drugs Product(s):	• Revuforj (revumenib)
FDA-Approved Indication(s):	• Treatment of relapsed or refractory (R/R) acute leukemia with a lysine methyltransferase 2A gene (*KMT2A*) translocation in adult and pediatric patients 1 year and older.

Background:	• Revumenib is a menin inhibitor and blocks the interaction of both wild-type KMT2A and KMT2A fusion proteins with menin thus altering the transcription of multiple genes including differentiation markers. • Leukemia is a common blood and bone marrow cancer. The American Cancer Society (ACS) estimates that in 2024, 62,770 new people will be diagnosed with leukemia and there will be 23,670 deaths. Leukemia is the 11th most frequently diagnosed cancer and is categorized as acute or chronic. Chronic leukemias include chronic lymphocytic leukemia (CLL) and chronic myeloid leukemia (CML), while acute leukemias include acute myeloid leukemia (AML), acute lymphocytic leukemia (ALL) and mixed phenotype acute leukemia (MPAL). AML most commonly affects adults, with an average age at diagnosis of 69. In 2024, approximately 20,800 adults will be diagnosed with AML, with an estimated 11,220 deaths, accounting for roughly one-third of adult leukemia cases. ALL is estimated to cause 6,550 new cases and 1,330 deaths, predominantly affecting children under five. MPAL represents about 2-5% of acute leukemia cases. Five-year survival rates are 31.9% for AML, 72.0% for ALL and 70% for MPAL. • Approximately 10% of all leukemias involve KMT2A rearrangements, a mutation most prevalent in infants and children, associated with a much lower five-year survival rate around 25%. Over 95% of patients with KMT2A-rearranged acute leukemia exhibit a KMT2A translocation. According to the National Comprehensive Cancer Network (NCCN) AML Version 3.2024 and ALL Version 2.2024 Guidelines, the diagnosis of KMT2A rearrangement is a poor prognosis in adults and a high-risk group in pediatrics.

- The NCCN AML Version 3.2024 and ALL Version 2.2024 Guidelines, recommends chemotherapy, targeted therapy followed by hematopoietic stem-cell transplantation (HSCT) or clinical trials for treatment of R/R acute leukemia.
- There are currently no FDA approved diagnostic tools for the detection of a KMT2A translocation. The current process in identifying KMT2A translocations include pre-screening steps of cytogenic analyses, split-signal fluorescence in situ hybridization (FISH), RT-PCR or RNA-Seq at diagnostic centers.
- See Table 1 for the recommended dosing for patients ≥ 1 year old.
- **Table 1. Dosage for patients ≥ 1 year old**

Patients 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/m2 orally twice daily*

*See Table 2 for the total tablet dosage by body surface area (BSA) for patients weighing < 40 kg.

- **Table 2. Dosage for Patients Weighing < 40kg**

BSA (m^2)	Dosage for 160 mg/m^2	Dosage for 95 mg/m^2
1.4	220 mg twice daily	135 mg twice daily
1.3	220 mg twice daily	135 mg twice daily
1.2	185 mg twice daily	110 mg twice daily
1.1	185 mg twice daily	110 mg twice daily
1.0	160 mg twice daily	100 mg twice daily
0.9	135 mg twice daily	75 mg twice daily
0.8	135 mg twice daily	75 mg twice daily
0.7	110 mg twice daily	50 mg twice daily
0.6	100 mg twice daily	50 mg twice daily
0.5	75 mg twice daily	50 mg twice daily
0.4	50 mg twice daily	25 mg twice daily

- If needed, attain the desired dose by combining different strengths.
- Examples of CYP3A4 inhibitors include grapefruit, protease inhibitors, azole antifungals, cyclosporin, cimetidine, cobicistat, macrolides, amiodarone, or non-DHP calcium channel blockers.
- Prescribing Considerations:
    - Patients should 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.
    - Revuforj should be administered twice daily, either on an empty stomach or with a low-fat meal, at roughly the same time each day.
    - Revuforj has a black box warning for differentiation syndrome.
    - Revuforj has warnings and precautions for use in QTc interval prolongation and embryo-fetal toxicity.
    - Advice women not to breastfeed during treatment and for 1 week after last dose.
    - Patients taking a strong CYP3A4 inhibitor should reduce the Revuforj dose.
    - Patient should avoid taking strong or moderate CYP3A4 inducers when taking with Revuforj.
    - If a patient requires a treatment regimen that cannot be achieved using the available tablet strengths, the tablet may be crushed and dispersed in 20 mL of water, as instructed in the package insert, to obtain the desired dose.

Approval Criteria

I. Initial Authorization
When a benefit, coverage of Revuforj may be approved when all of the following criteria are met **(A., B., and C.)**:
- **A.** The member is 1 year of age or older.
- **B.** The member has a diagnosis of acute leukemia (ICD-10: C91.0, C92.0, C93.0, C94.0, C95.0), classified as relapsed or refractory.
- **C.** The member has a KMT2A gene translocation.

II. Reauthorization
When a benefit, reauthorization of Revuforj may be approved when the following criterion is met **(A.)**:
- **A.** The prescriber attests that the member is tolerating therapy and has experienced a therapeutic response defined as one (1) of the following **(1. or 2.):**
  - **1.** Disease improvement
  - **2.** Delayed disease progression

III. An exception to some or all of the criteria above may be granted for select members and/or circumstances based on state and/or federal regulations.

IV. Coverage of oncology drug(s) listed in this policy may be approved on a case-by-case basis per indications supported in the most current NCCN guidelines.

Limitations of Coverage

I. Coverage of drug(s) addressed in this policy for disease states outside of the FDA-approved indications should be denied based on the lack of clinical data to support effectiveness and safety in other conditions unless otherwise noted in the approval criteria.
II. For Commercial or HCR members with a closed formulary, a non-formulary product will only be approved if the member meets the criteria for a formulary exception in addition to the criteria outlined within this policy.

Authorization Duration

- Commercial and HCR Plans: If approved, up to a 12 authorization may be granted.

Automatic Approval Criteria

None

References:

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14. Meyer C, Larghero P, Almeida Lopes B, et al. The KMT2A recombinome of acute leukemias in 2023. Leukemia. 2023;37(5):988-1005.