Clinical Policy: Revumenib (Revuforj)

Reference Number: CP.PHAR.707
Effective Date: 03.01.25
Last Review Date: 02.25
Line of Business: Commercial, HIM, Medicaid

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Revumenib (Revuforj®) is a menin inhibitor.

FDA Approved Indication(s)

Revuforj is 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.

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that Revuforj is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Acute Leukemia (must meet all)**:**

1. Diagnosis of relapsed or refractory acute leukemia (e.g., acute myeloid leukemia [AML], acute lymphoblastic leukemia [ALL], and mixed phenotype acute leukemia [MPAL]);
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Age ≥ 1 year;
4. Disease is positive for a KMT2A gene translocation;
5. For Revuforj requests, member must use revumenib, if available, unless contraindicated or clinically significant adverse effects are experienced;
6. Request meets one of the following (a or b):*
   a. Dose does not exceed one of the following (i or ii):
      i. Weight ≥ 40 kg: both of the following (1 and 2):
         1) 540 mg per day;
         2) 4 tablets per day;
      ii. Weight < 40 kg: 160 mg/m^2 (*see Section V: Dosage and Administration for recommended dosage regimen);*
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration: 6 months

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. Acute Leukemia (must meet all)**:**
1. Currently receiving medication via Centene benefit, or documentation supports that member is currently receiving Revuforj for a covered indication and has received this medication for at least 30 days;
2. Member is responding positively to therapy;
3. For Revuforj requests, member must use revumenib, if available, unless contraindicated or clinically significant adverse effects are experienced;
4. If request is for a dose increase, request meets one of the following (a or b):*
   a. Dose does not exceed one of the following (i or ii):
      i. Weight ≥ 40 kg: both of the following (1 and 2):
         1) 540 mg per day;
         2) 4 tablets per day;
      ii. Weight < 40 kg: 160 mg/m^2 (*see Section V: Dosage and Administration for recommended dosage regimen);*
   b. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or

b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or

2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

ALL: acute lymphoblastic leukemia
AML: acute myeloid leukemia
BSA: body surface area
MPAL: mixed phenotype acute leukemia
NCCN: National Comprehensive Cancer Network
FDA: Food and Drug Administration

Appendix B: Therapeutic Alternatives

Not applicable

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): none reported
- Boxed warning(s): differentiation syndrome

Appendix D: General Information

- Examples of strong CYP3A4 inhibitors: posaconazole, itraconazole, voriconazole

V. Dosage and Administration

<table>
<tr><th>Indication</th><th>Dosing Regimen</th><th>Maximum Dose</th></tr>
<tr><td>Acute leukemia</td><td>The recommended dosage varies by patient weight and concomitant use of strong CYP3A4 inhibitors:
<table>
<tr><th>Weight</th><th>Without strong CYP3A4 inhibitors</th><th>With strong CYP3A4 inhibitors</th></tr>
<tr><td>≥ 40 kg</td><td>270 mg PO BID</td><td>160 mg PO BID</td></tr>
<tr><td>< 40 kg</td><td>160 mg/m^2 PO BID*</td><td>95 mg/m^2 PO BID*</td></tr>
</table>
*See table below for recommended tablet dosage by BSA for patients weighing less than 40 kg</td><td>See regimen</td></tr>
</table>

Indication	Dosing Regimen	Maximum Dose
	Recommended dosage for patients weighing < 40 kg by body surface area (BSA):	

BSA (m^2)	Without strong CYP3A4 inhibitors (160 mg/m^2)	With strong CYP3A4 inhibitors (95 mg/m^2)
1.4	220 mg PO BID	135 mg PO BID
1.3	220 mg PO BID	135 mg PO BID
1.2	185 mg PO BID	110 mg PO BID
1.1	185 mg PO BID	110 mg PO BID
1	160 mg PO BID	100 mg PO BID
0.9	135 mg PO BID	75 mg PO BID
0.8	135 mg PO BID	75 mg PO BID
0.7	110 mg PO BID	50 mg PO BID
0.6	100 mg PO BID	50 mg PO BID
0.5	75 mg PO BID	50 mg PO BID
0.4	50 mg PO BID	25 mg PO BID

VI. Product Availability

Tablets: 25 mg, 110 mg, 160 mg

VII. References

1. Revuforj Prescribing Information. Waltham, MA: Syndax Pharmaceuticals, Inc.; November 2024. Available at: https://revuforjhcp.com/. Accessed November 26, 2024.
2. National Comprehensive Cancer Network. Acute Lymphoblastic Leukemia. Version 2.2024. Available at: https://www.nccn.org/professionals/physician_gls/pdf/all.pdf. Accessed November 26, 2024.
3. National Comprehensive Cancer Network. Acute Myeloid Leukemia. Version 3.2024. Available at: https://www.nccn.org/professionals/physician_gls/pdf/aml.pdf. Accessed November 26, 2024.
4. National Comprehensive Cancer Network. Pediatric Acute Myeloid Leukemia. Version 1.2025. Available at: https://www.nccn.org/professionals/physician_gls/pdf/ped_all.pdf. Accessed November 26, 2024.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	11.26.24	02.25

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical

policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions, and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members, and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.