Clinical Policy: Mavorixafor (Xolremdi)

Reference Number: CP.PHAR.679
Effective Date: 07.01.24
Last Review Date: 05.25
Line of Business: Commercial, HIM, Medicaid

Revision Log

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

Description

Mavorixafor (Xolremdi™) is a CXC chemokine receptor 4 (*CXCR4*) antagonist.

FDA Approved Indication(s)

Xolremdi is indicated in patients 12 years of age and older with WHIM syndrome (warts, hypogammaglobulinemia, infections and myelokathexis) to increase the number of circulating mature neutrophils and lymphocytes.

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 Xolremdi is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. WHIM Syndrome (must meet all)**:**

1. Diagnosis of WHIM syndrome confirmed by genetic confirmation of a *CXCR4* variant;
2. Prescribed by or in consultation with a geneticist, hematologist, immunologist, or infectious disease specialist;
3. Age ≥ 12 years;
4. Baseline absolute neutrophil count (ANC) is ≤ 400 cells/µL;
5. Documentation of member's baseline absolute lymphocyte count (ALC) and number of infections experienced within the last year;
6. Xolremdi is not prescribed concurrently with plerixafor (Mozobil®);
7. Documentation of member's current weight (in kg);
8. Dose does not exceed any of the following:
   a. Weight > 50 kg: 400 mg (4 capsules) per day;
   b. Weight ≤ 50 kg: 300 mg (3 capsules) per day.

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. WHIM Syndrome (must meet all)**:**

1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B)*;
2. Member is responding positively to therapy as evidenced by both of the following (a and b):
   a. At least two instances of an ANC ≥ 500 cells/μL, on two separate days within the last six months;
   b. One of the following (i or ii):
      i. At least two instances of an ALC ≥ 1,000 cells/μL, on two separate days within the last six months;
      ii. Reduction from baseline in infections;
3. Xolremdi is not prescribed concurrently with plerixafor (Mozobil®);
4. Documentation of member's current weight (in kg);
5. If request is for a dose increase, new dose does not exceed any of the following:
   a. Weight > 50 kg: 400 mg (4 capsules) per day;
   b. Weight ≤ 50 kg: 300 mg (3 capsules) per day.

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

ALC: absolute lymphocyte count
ANC: absolute neutrophil count
CXCR4: CXC chemokine receptor 4
FDA: Food and Drug Administration
WHIM: warts, hypogammaglobulinemia, infections and myelokathexis

Appendix B: Therapeutic Alternatives

Not applicable

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): concomitant use with drugs that are highly dependent on CYP2D6 for clearance
- Boxed warning(s): none reported

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
WHIM syndrome	Weight-based dosing: • > 50 kg: 400 mg PO QD • ≤ 50 kg: 300 mg PO QD	400 mg/day

VI. Product Availability

Capsule: 100 mg

VII. References

1. Xolremdi Prescribing Information. Boston, MA: X4 Pharmaceuticals, Inc.; September 2024. Available at: https://xolremdihcp.com/pdf/prescribing-information.pdf. Accessed January 21, 2025.
2. Badolato R, Alsina L, Azar A, et al. Phase 3 randomized trial of mavorixafor, CXCR4 antagonist, in WHIM syndrome. Blood 2024 Apr 21; blood.2023022658. doi:10.1182/blood.2023022658. Online ahead of print.

3. Badolato R, 4WHIM Study Group, Hu Y, et al. Results of a phase 3 trial of an oral CXCR4 antagonist, mavorixafor, for the treatment of participants with WHIM syndrome: investigational assessment of lymphocyte subpopulations in peripheral blood. J Allergy Clin Immunol 2024;153(2):AB143. https://doi.org/10.1038/s41435-022-00181-9.
4. Zmajkovicova K, Pawar S, Maier-Munsa S, et al. Genotype-phenotype correlations in WHIM syndrome: a systematic characterization of *CXCR4*^{WHIM} variants. Genes & Immunity 2022;23:196-204. https://doi.org/10.1038/s41435-022-00181-9.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	05.16.24	06.24
2Q 2025 annual review: no significant changes; references reviewed and updated.	01.21.25	05.25

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.