Pharmacy Policy Bulletin: J-1381 Xolremdi (mavorixafor) – Commercial and Healthcare Reform	
Number: J-1381	**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-1381-002	**Original Date:** 06/05/2024
Effective Date: 07/18/2025	**Review Date:** 06/25/2025

Drugs Product(s):	• Xolremdi (mavorixafor)
FDA-Approved Indication(s):	• To increase the number of circulating mature neutrophils and lymphocytes in patients 12 years of age and older with WHIM syndrome (warts, hypogammaglobulinemia, infections, and myelokathexis).

Background:	• Xolremdi is a CXCR4 antagonist that blocks the binding of CXC Chemokine Ligand 12 (CXCL12) to the CXCR4 receptor. CXCR4 regulates movement of leukocytes to and from the bone marrow. In WHIM syndrome, autosomal dominant mutations in the CXCR4 receptor gene lead to increased responsiveness to CXCL12. This causes retention of white blood cells in bone marrow. Treatment with Xolremdi increases the mobilization of neutrophils and lymphocytes from the bone marrow to the peripheral circulation in patients with WHIM syndrome, which decreases susceptibility to viral and bacterial infections. • WHIM syndrome is a rare primary immunodeficiency disorder impacting approximately 1,000 patients in the United States (US). Patients have increased susceptibility to infections; symptoms first appear in early childhood with repeated middle ear infections, cellulitis, bacterial pneumonia, sinusitis, septic arthritis, dental cavities, or periodontitis. These patients typically contract human papillomavirus (HPV) in their teens, causing warts on the hands, face, feet, and trunk. Warts may also develop on mucosal membranes or on the genitals, and these particular warts are associated with an increased risk of progressing into carcinomas. • Patients usually have a high level of neutrophils and lymphocytes in the bone marrow (myelokathexis) as these cells mature and die before being released into the circulatory system. This causes neutropenia, lymphocytopenia, and low levels of immunoglobulins. Patients can live well into adulthood but have an increased risk of cancer. • In clinical trials of Xolremdi, enrolled patients had a genotype-confirmed variant of CXCR4 consistent with WHIM syndrome and a confirmed absolute neutrophil count (ANC) ≤ 400 cells/µL.

	• ICD-10 Code Information:
	  ○ ICD-10: D81.8 “Other combined immunodeficiencies” may apply to Xolremdi; however, the prescriber must confirm that the member has a specific diagnosis of WHIM syndrome.
	  ○ ICD-10: D89.9 “Disorder involving the immune mechanism, unspecified” may apply to Xolremdi; however, the prescriber must confirm that the member has a specific diagnosis of WHIM syndrome.
	• Prescribing Considerations:
	  ○ Xolremdi can cause embryo-fetal toxicity and should not be used in pregnant patients.
	  ○ Xolremdi is contraindicated for use in patients with concurrently taking drugs highly dependent on CYP2D6 for clearance.

Approval Criteria

I. Initial Authorization

When a benefit, coverage of Xolremdi may be approved when all of the following criteria are met **(A., B., and C.):**

A. The member is 12 years of age or older.

B. The member has a diagnosis of WHIM syndrome (warts, hypogammaglobulinemia, infections, and myelokathexis) (No ICD-10).

C. The provider submits documentation of both of the following **(1. and 2):**

1. The member has a genotype-confirmed variant of CXCR4.

2. The member has an absolute neutrophil count (ANC) ≤ 400 cells/µL.

II. Reauthorization

When a benefit, reauthorization of Xolremdi may be approved when the following criterion is met **(A.)**:

A. The prescriber attests that the member has experienced a reduction in the incidence of infections.

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.

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 month authorization may be granted.

Automatic Approval Criteria

None

References:

1. Xolremdi [package insert]. Boston, MA: X4 Pharmaceuticals; April 2024.
2. Rare Diseases. WHIM Syndrome. Available at: https://rarediseases.org/rare-diseases/whim-syndrome/#disease-overview-main. Accessed May 15, 2025.
3. Orphanet. WHIM Syndrome. Available at: https://www.orpha.net/en/disease/detail/51636. Accessed May 15, 2025.
4. DynaMed. WHIM Syndrome. Available at: https://www.dynamed.com/condition/whim-syndrome. Accessed May 15, 2025.
5. Bonilla FA, Khan DA, Ballas ZK, et al. Practice parameter for the diagnosis and management of primary immunodeficiency. *J Allergy Clin Immunol.* 2015 Nov;136(5):1186-205.e1-78.

Pharmacy policies do not constitute medical advice, nor are they intended to govern physicians' prescribing or the practice of medicine. They are intended to reflect the plan's coverage and reimbursement guidelines. Coverage may vary for individual members, based on the terms of the benefit contract.

The plan retains the right to review and update its pharmacy policy at its sole discretion. These guidelines are the proprietary information of the plan. Any sale, copying or dissemination of the pharmacy policies is prohibited; however, limited copying of pharmacy policies is permitted for individual use.