



PRIOR AUTHORIZATION POLICY

- POLICY:** Complement System Disorders – WHIM Syndrome – Xolremdi Prior Authorization Policy
- Xolremdi™ (mavorixafor capsules – X4 Pharmaceuticals)

REVIEW DATE: 05/08/2024

INSTRUCTIONS FOR USE

THE FOLLOWING COVERAGE POLICY APPLIES TO HEALTH BENEFIT PLANS ADMINISTERED BY CIGNA COMPANIES. CERTAIN CIGNA COMPANIES AND/OR LINES OF BUSINESS ONLY PROVIDE UTILIZATION REVIEW SERVICES TO CLIENTS AND DO NOT MAKE COVERAGE DETERMINATIONS. REFERENCES TO STANDARD BENEFIT PLAN LANGUAGE AND COVERAGE DETERMINATIONS DO NOT APPLY TO THOSE CLIENTS. COVERAGE POLICIES ARE INTENDED TO PROVIDE GUIDANCE IN INTERPRETING CERTAIN STANDARD BENEFIT PLANS ADMINISTERED BY CIGNA COMPANIES. PLEASE NOTE, THE TERMS OF A CUSTOMER'S PARTICULAR BENEFIT PLAN DOCUMENT [GROUP SERVICE AGREEMENT, EVIDENCE OF COVERAGE, CERTIFICATE OF COVERAGE, SUMMARY PLAN DESCRIPTION (SPD) OR SIMILAR PLAN DOCUMENT] MAY DIFFER SIGNIFICANTLY FROM THE STANDARD BENEFIT PLANS UPON WHICH THESE COVERAGE POLICIES ARE BASED. FOR EXAMPLE, A CUSTOMER'S BENEFIT PLAN DOCUMENT MAY CONTAIN A SPECIFIC EXCLUSION RELATED TO A TOPIC ADDRESSED IN A COVERAGE POLICY. IN THE EVENT OF A CONFLICT, A CUSTOMER'S BENEFIT PLAN DOCUMENT ALWAYS SUPERSEDES THE INFORMATION IN THE COVERAGE POLICIES. IN THE ABSENCE OF A CONTROLLING FEDERAL OR STATE COVERAGE MANDATE, BENEFITS ARE ULTIMATELY DETERMINED BY THE TERMS OF THE APPLICABLE BENEFIT PLAN DOCUMENT. COVERAGE DETERMINATIONS IN EACH SPECIFIC INSTANCE REQUIRE CONSIDERATION OF 1) THE TERMS OF THE APPLICABLE BENEFIT PLAN DOCUMENT IN EFFECT ON THE DATE OF SERVICE; 2) ANY APPLICABLE LAWS/REGULATIONS; 3) ANY RELEVANT COLLATERAL SOURCE MATERIALS INCLUDING COVERAGE POLICIES AND; 4) THE SPECIFIC FACTS OF THE PARTICULAR SITUATION. EACH COVERAGE REQUEST SHOULD BE REVIEWED ON ITS OWN MERITS. MEDICAL DIRECTORS ARE EXPECTED TO EXERCISE CLINICAL JUDGMENT AND HAVE DISCRETION IN MAKING INDIVIDUAL COVERAGE DETERMINATIONS. COVERAGE POLICIES RELATE EXCLUSIVELY TO THE ADMINISTRATION OF HEALTH BENEFIT PLANS. COVERAGE POLICIES ARE NOT RECOMMENDATIONS FOR TREATMENT AND SHOULD NEVER BE USED AS TREATMENT GUIDELINES. IN CERTAIN MARKETS, DELEGATED VENDOR GUIDELINES MAY BE USED TO SUPPORT MEDICAL NECESSITY AND OTHER COVERAGE DETERMINATIONS.

CIGNA NATIONAL FORMULARY COVERAGE:

OVERVIEW

Xolremdi, a CXC chemokine receptor 4 (CXCR4) antagonist, is indicated for the treatment of **WHIM syndrome** (warts, hypogammaglobulinemia, infections and myelokathexis) to increase the number of circulating mature neutrophils and lymphocytes in adults and children ≥ 12 years of age.¹

Disease Overview

WHIM syndrome is a rare autosomal primary immunodeficiency that causes hyperactivity with failure to down regulate the CXCR4 receptor.^{2,3} Most of the patients with WHIM syndrome are heterozygous carriers of mutations of CXCR4. Clinical presentation include recurrent bacterial infections and severe or chronic neutropenia that begins in infancy or early childhood. There is no cure for WHIM syndrome and prior to the approval of Xolremdi, treatment was based on patient's symptoms.²

Clinical Efficacy

The efficacy of Xolremdi for the treatment of WHIM syndrome has been evaluated in one pivotal study.^{1,4} The study included patients ≥ 12 years of age with genetically confirmed WHIM syndrome and confirmed absolute neutrophil count

(ANC) \leq 400 cells/ μ L or white blood cells (WBC) \leq 400 cells/ μ L. The primary efficacy endpoint of the meantime above threshold ANC (TAT-ANC) at Week 52 assessment.

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of Xolremdi. All approvals are provided for the duration noted below. In cases where the approval is authorized in months, 1 month is equal to 30 days. Because of the specialized skills required for evaluation and diagnosis of patients treated with Xolremdi as well as the monitoring required for adverse events and long-term efficacy, initial approval requires Xolremdi to be prescribed by or in consultation with a physician who specializes in the condition being treated.

• **Xolremdi™ (mavorixafor capsules – X4 Pharmaceuticals)**
is(are) covered as medically necessary when the following criteria is(are) met for FDA-approved indication(s) or other uses with supportive evidence (if applicable):

FDA-Approved Indication

- 1. WHIM syndrome.** Approve Xolremdi for the duration noted if the patient meets ONE of the following (A or B):
 - A) Initial Therapy.** Approve for 1 year if the patient meets ALL of the following (i, ii, iii, and iv):
 - i.** Patient is \geq 12 years of age; AND
 - ii.** Genetic testing confirms pathogenic and or likely pathogenic variants in the CXCR4 gene; AND
 - iii.** Patient meets ONE of the following (a or b):
 - a)** At baseline, patient had an absolute neutrophil count \leq 400 cells/ μ L; OR
 - b)** At baseline, patient had a white blood cell count \leq 400 cells/ μ L; AND
 - iv.** The medication is prescribed by or in consultation with an immunologist, hematologist or dermatologist.
 - B) Patient is Currently Receiving Xolremdi.** Approve for 1 year if, according to the prescriber, the patient is continuing to derive benefit from Xolremdi as determined by the most recent objective measurement.
Note: Examples of objective measurements of a response to Xolremdi therapy are reduced frequency, duration, or severity of infections, less frequent treatment with antibiotics, fewer warts, or improved or stabilized clinical signs/symptoms of WHIM syndrome (e.g., absolute neutrophil count, white blood cell count, and absolute lymphocyte count).

CONDITIONS NOT COVERED

- **Xolremdi™ (mavorixafor capsules – X4 Pharmaceuticals)**

is(are) considered experimental, investigational or unproven for ANY other use(s) (criteria will be updated as new published data are available).

REFERENCES

1. Xolremdi™ oral capsules [prescribing information]. Boston, MA: X4 Pharmaceuticals; April 2024.
2. Kawai T and Malech HL. WHIM syndrome: congenital immune deficiency disease. *Curr Opin Hematol.* 2009;16(1):20-26.
3. Heusinkveld LE, Yim E, Yant A, et al. Pathogenesis, diagnosis and therapeutic strategies in WHIM syndrome immunodeficiency. *Expert Opin Orphan Drugs.* 2017;5(10):813-825.
4. Badolato R, Donadieu J, and 4WHIM Study Group. Results of a phase 3 Trial of an oral CXCR4 antagonist, mavoxixafor, for treatment of patients with WHIM syndrome. Presented at: Clinical Immunology Society Annual Meeting and European Hematology Association Annual Congress; *Clin Immun.* 2023;250S.

HISTORY

Type of Revision	Summary of Changes	Review Date
New Policy		05/08/2024

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