Xolremdi® (mavorixafor)

BENEFIT APPLICATION

Benefit determinations are based on the applicable contract language in effect at the time the services were rendered. Exclusions, limitations or exceptions may apply. Benefits may vary based on contract, and individual member benefits must be verified. Wellmark determines medical necessity only if the benefit exists and no contract exclusions are applicable. This medical policy may not apply to FEP. Benefits are determined by the Federal Employee Program.

DESCRIPTION

The indications below including FDA-approved indications and compendial uses are considered covered benefits provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
Xolremdi is a CXC chemokine receptor 4 antagonist 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

Required Documentation
Submission of the following information is necessary to initiate the prior authorization review:

1. Initial Requests:
   A. Chart notes or medical records documenting a diagnosis of WHIM syndrome confirmed by genotype variant of *CXCR4*
   B. Chart notes or medical records documenting baseline absolute neutrophil count (ANC)
   C. Chart notes or medical records documenting symptoms and complications associated with WHIM syndrome
2. Continuation Requests: Chart notes, laboratory values or medical records documenting disease stability or improvement

Prescriber Specialties
The requested medication must be prescribed by or in consultation with one of the following:

1. Immunologist
2. Hematologist

Criteria for Initial Approval

WHIM syndrome

Authorization of 6 months may be granted to members 12 years of age and older for treatment of WHIM syndrome when all of the following criteria are met:

1. Diagnosis of WHIM syndrome genotype-confirmed variant of CXCR4 gene consistent with WHIM syndrome
2. Baseline absolute neutrophil count (ANC) ≤400 cells/μL
3. Clinical manifestations of disease consistent with WHIM syndrome (e.g., repeated bacterial infections, persistent warts)

Continuation of Therapy

WHIM syndrome

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization and demonstrating a positive response to therapy based on any of the following:

1. Reduced infection frequency relative to pretreatment
2. Reduction of warts on the skin and genital warts
3. Increased absolute neutrophil count (ANC) and/or absolute lymphocyte count (ALC) relative to baseline

Other

Xolremdi (mavorixafor) is considered **not medically necessary** for members who do not meet the criteria set forth above.

Members currently receiving the requested medication as samples or via the manufacturer's patient assistance program will be required to meet the criteria for initial approval. This ensures that members are treated equally regardless of their provider's ability to access medication samples.

Dosing and Administration

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines.

Quantity Limits Apply

Medication	Standard Limit	FDA Recommended Dosing
Xolremdi (mavorixafor) 100 mg capsule	120 capsules per 30 days	• Weight >50 kg: 400 mg orally once daily • Weight ≤50 kg: 300 mg orally once daily

CLINICAL RATIONALE

Warts, hypogammaglobulinemia, infections and myelokathexis (WHIM) syndrome is an ultra-rare, combined primary immunodeficiency. Hypogammaglobulinemia is a deficiency in specific infection-fighting antibodies in the blood, and myelokathexis refers to the failure of neutrophils to move from the bone marrow into the bloodstream.

WHIM syndrome is caused by genetic variations in the CXCR4 receptor, which is a key regulator of the mobilization of white blood cells (neutrophils and lymphocytes). Patients with WHIM syndrome may also have trouble with distributing other types of immune cells to the blood and as a result, are predisposed to frequent viral and bacterial infections, skin and genital warts, and are at an increased risk of developing

cancer caused by human papillomavirus (HPV). WHIM syndrome is inherited in an autosomal-dominant pattern. Some individuals with the characteristic symptoms of WHIM syndrome do not have a detectable mutation in the CXCR4 gene, which suggests that the disorder may have other genetic causes. The majority of patients identified with WHIM syndrome, however, do have this detectable mutation.

Some patients have mild expression of WHIM syndrome while others develop potentially life-threatening complications. Symptoms often develop in early childhood, with children experiencing repeated bacterial infections that can be mild or severe but usually respond promptly to antibiotic therapy. However, chronic infections can potentially lead to additional complications (e.g. chronic ear infections and hearing loss, dental infection and tooth loss, pneumonia and bronchiectasis, atelectasis, and respiratory/heart failure).

WHIM syndrome is an extremely rare disorder, and its exact prevalence or incidence in the general population is unknown, although it has been estimated at about 0.2 per million live births. Approximately 100 cases have been reported in medical literature. It is estimated that fewer than one in four patients present with all four manifestations of the disease (warts, hypogammaglobulinemia, infections, and myelokathexis), which makes diagnosis difficult. Due to complications, patients may have a lower life expectancy compared to the general population.

Diagnosis of WHIM syndrome is made based on symptoms, patient history, clinical testing (complete blood count with differential showing neutropenia, variable degree of lymphopenia, hypogammaglobulinemia, etc.) and genetic tests. Patients with recurrent bacterial infections, neutropenia, and warts should be tested for WHIM syndrome. If WHIM syndrome is suspected, a bone marrow biopsy may be performed that could reveal myelokathexis, which strongly suggests WHIM syndrome. Molecular genetic testing is also available.

Current treatment options only address symptoms of the disease. Colony stimulating factors, immunoglobulins, and anti-infectives have been used in a supportive capacity based on the patient's specific clinical picture. Plerixafor has also been used off label with mixed results.

PROCEDURES AND BILLING CODES

To report provider services, use appropriate CPT* codes, Alpha Numeric (HCPCS level 2) codes, Revenue codes, and/or ICD diagnostic codes.

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POLICY HISTORY

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