

Orladeyo (berotralstat)

Disclaimer

Clinical guidelines are developed and adopted to establish evidence-based clinical criteria for utilization management decisions. Clinical guidelines are applicable according to policy and plan type. The Plan may delegate utilization management decisions of certain services to third parties who may develop and adopt their own clinical criteria.

Coverage of services is subject to the terms, conditions, and limitations of a member's policy, as well as applicable state and federal law. Clinical guidelines are also subject to in-force criteria such as the Centers for Medicare & Medicaid Services (CMS) national coverage determination (NCD) or local coverage determination (LCD) for Medicare Advantage plans. Please refer to the member's policy documents (e.g., Certificate/Evidence of Coverage, Schedule of Benefits, Plan Formulary) or contact the Plan to confirm coverage.

Summary

Orladeyo (berotralstat) is FDA-approved for prophylaxis to prevent attacks of hereditary angioedema (HAE) in adults and pediatric patients 12 years of age and older. HAE is a rare disease that causes swelling, pain and inflammation in various areas of the body including the face, hands, feet, throat, stomach, and bowels. HAE can be caused by a reduced amount or decreased function of C1 esterase inhibitor protein, a regulator of inflammatory pathways.

The recommended dosage for Orladeyo (berotralstat) is 150 mg taken orally once daily. It is available as 150 mg and 110 mg capsules because dosage may need to be adjusted for certain patients (e.g., with moderate or severe hepatic impairment, with chronic administration of P-glycoprotein or breast cancer resistance protein (BCRP) inhibitors, or with persistent gastrointestinal reactions). Alternatives for Orladeyo (berotralstat) include products such as Takhzyro, Haegarda, Cinryze, or Danazol.

NOTE: The Plan requires that members be unable to use, or have tried and failed preferred product(s) first. Requests for non-formulary medications are also subject to Medical Necessity Criteria for Non-Formulary Drugs (PG069).

Definitions

“**C1 inhibitor**” refers to an enzyme that functions as a major anti-inflammatory **protein** in the body. People who have HAE have low levels of **C1 inhibitor** in their body.

“**C4**” or “**Complement 4**” refers to an enzyme that is involved in the inflammatory response. Alterations in C1 inhibitor can result in low levels of C4 in people who have HAE.

“**Hereditary angioedema (HAE)**” refers to a rare, inherited disease that causes swelling, pain and inflammation in various areas of the body including the face, hands, feet, throat, stomach, and bowels.

Medical Necessity Criteria for Initial Authorization

The Plan considers **Orladeyo (berotralstat)** medically necessary when **ALL** of the following criteria are met:

1. Prescribed by or in consultation with an allergist, hematologist, immunologist, or other specialist experienced in the diagnosis and management of hereditary angioedema (HAE); **AND**
2. The member is 12 years of age or older; **AND**
3. Is being used for prevention of attacks of hereditary angioedema (HAE), confirmed by **ONE** of the following:
 - a. clinically appropriate low levels (as defined by the laboratory reference values) of **BOTH**:
 - i. low complement C4 (either at baseline or during an attack); **and**
 - ii. low C1 esterase inhibitor (C1-INH) antigenic protein level (Type 1 HAE) **OR** functional level (Type 2 HAE); **or**
 - b. Documented normal or near normal C4, C1-INH antigen, and C1-INH function **AND ONE** of the following:
 - i. Demonstration of a mutation (e.g., in the factor XII, plasminogen, angiotensin-converting enzyme 1, or kininogen gene) associated with HAE; **or**
 - ii. A positive family history of recurrent angioedema and documented lack of efficacy of high-dose antihistamine therapy (e.g., cetirizine at 40 mg/day or the equivalent); **AND**
4. The member has a documented history of moderate or severe attacks of hereditary angioedema (e.g., airway swelling, severe abdominal pain, facial swelling, nausea and vomiting, painful facial distortion); **AND**
5. Dosage is within the recommended limit of 150 mg (taken orally) once daily; **AND**
6. Chart documentation and supporting laboratory test results are provided for review to substantiate the above listed requirements.

If the above prior authorization criteria are met, Orladeyo (berotralstat) will be approved for 12-months.

Medical Necessity Criteria for Reauthorization

Reauthorization for 12 months will be granted if **BOTH** of the following are met:

1. the member still meets all applicable initial criteria; **AND**
2. chart documentation shows the member has experienced a positive clinical response to therapy as evidenced by **ONE** of the following compared to baseline (prior to starting prophylaxis therapy):
 - a. At least a (\geq) 50% reduction in frequency of acute HAE attacks; **or**
 - b. Reduction in severity, duration, or need for rescue medication of acute HAE attacks.

Experimental or Investigational / Not Medically Necessary

Orladeyo (berotralstat) for any other indication is considered not medically necessary by the Plan, as it is deemed to be experimental, investigational, or unproven.

References

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3. Jose J, Zacharias J, Craig T. Review of select practice parameters, evidence-based treatment algorithms, and international guidelines for hereditary angioedema. *Clinical Reviews in Allergy and Immunology* 2016;51(2):193-206. DOI: 10.1007/s12016-016-8546-7.
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Clinical Guideline Revision / History Information

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