Cigna National Formulary Coverage Policy

Prior Authorization
Hereditary Angioedema – Orladeyo® (berotralstat capsules)

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Product Identifier(s)

79815, 79818

INSTRUCTIONS FOR USE

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National Formulary Medical Necessity

Cigna covers berotralstat (Orladeyo®) as medically necessary when the following criteria are met for FDA Indications or Other Uses with Supportive Evidence:

Prior Authorization is recommended for prescription benefit coverage of Orladeyo. Because of the specialized skills required for evaluation and diagnosis of individuals with this condition, approval requires Orladeyo to be prescribed by or in consultation with a physician who specializes in the condition being treated. All approvals are provided for the duration noted below.

Documentation: Documentation will be required where noted in the criteria as [documentation required]. Documentation may include, but is not limited to, chart notes, laboratory records, and prescription claims records.
1. **Hereditary Angioedema (HAE) Due to C1 Inhibitor (C1-INH) Deficiency [Type I or Type II] – Prophylaxis.** Approve Orladeyo for 1 year if the individual meets one the following criteria (A or B):

   **A) Initial therapy.** Approve if the individual meets all of the following criteria (i, ii, and iii):
   
   i. Individual is ≥ 12 years of age; AND
   
   ii. Individual has HAE type I or type II as confirmed by the following diagnostic criteria (a and b):

   - **Note:** A diagnosis of HAE with normal C1-INH (also referred to as HAE type III) does NOT satisfy this requirement.
   
   - a) Individual has low levels of functional C1-INH protein (< 50% of normal) at baseline, as defined by the laboratory reference values [documentation required]; AND
   
   - b) Individual has lower than normal serum C4 levels at baseline, as defined by the laboratory reference values [documentation required]; AND
   
   iii. The medication is prescribed by or in consultation with an allergist/immunologist or a physician who specializes in the treatment of HAE or related disorders.

   **B) Individual is currently receiving Orladeyo.** Approve if the individual meets all of the following criteria (i, ii, iii, and iv):

   i. Individual is ≥ 12 years of age; AND

   ii. Individual has a diagnosis of HAE type I or II [documentation required]; AND

   - **Note:** A diagnosis of HAE with normal C1-INH (also referred to as HAE type III) does NOT satisfy this requirement.

   iii. According to the prescriber, the individual has had a favorable clinical response since initiating Orladeyo prophylactic therapy compared with baseline (i.e., prior to initiating prophylactic therapy); AND

   - **Note:** Examples of favorable clinical response include decrease in HAE acute attack frequency, decrease in HAE attack severity, or decrease in duration of HAE attacks.

   iv. The medication is prescribed by or in consultation with an allergist/immunologist or a physician who specializes in the treatment of HAE or related disorders.

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### Conditions Not Covered

Berotralstat (Orladeyo®) is considered experimental, investigational or unproven for ANY other use including the following (this list may not be all inclusive):

1. **Concomitant Use with Other HAE Prophylactic Therapies (e.g., Cinryze, Haegarda, Takhzyro).**

   Orladeyo has not been studied in combination with other prophylactic therapies for HAE, and combination therapy for long-term prophylactic use is not recommended. Individuals may use other medications, including Cinryze, for on-demand treatment of acute HAE attacks, and for short-term (procedural) prophylaxis.

### Background

**Overview**

Orladeyo, an inhibitor of plasma kallikrein, is indicated for prophylaxis to prevent attacks of hereditary angioedema (HAE) in patients ≥ 12 years of age.¹

**Guidelines**

Orladeyo is not yet addressed in guideline recommendations, although positive Phase III data are recognized in guidelines from the US HAE Association Medical Advisory Board (2020).² According to those guidelines, when HAE is suspected based on clinical presentation, appropriate testing includes measurement of the serum C4 level, C1 esterase inhibitor (C1-INH) antigenic level, and C1-INH functional level.² Low C4 plus low C1-INH antigenic or functional level is consistent with a diagnosis of HAE types I/II. The decision on when to use long-term prophylaxis cannot be made on rigid criteria but should reflect the needs of the individual patient. First-line medications for HAE I/II include intravenous C1-INH, Haegarda® (C1-INH [human] subcutaneous injection), or Takhzyro® (lanadelumab-flyo subcutaneous injection). The guideline was written prior to approval of Orladeyo.
The International/Canadian HAE Guideline (2019) notes that plasma-derived C1-INH and Takhzyro are effective therapies for long-term prophylaxis in patients with HAE I/II (high level of evidence, strong recommendation).³

References


Revision History

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<thead>
<tr>
<th>Type of Revision</th>
<th>Summary of Changes</th>
<th>Approval Date</th>
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<tbody>
<tr>
<td>New Policy</td>
<td>--</td>
<td>12/09/2020</td>
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<tr>
<td>Annual Revision</td>
<td>No criteria changes.</td>
<td>01/05/2022</td>
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<tr>
<td>Selected Revision</td>
<td><strong>Hereditary Angioedema (HAE) Due to C1 Inhibitor (C1-INH) Deficiency [Type I or Type II] – Prophylaxis:</strong> A Note was added to initial and continuation criteria that a diagnosis of HAE with normal C1-INH (also known as HAE type III) does not satisfy the requirement for a diagnosis of HAE type I or type II.</td>
<td>06/01/2022</td>
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