Prior Authorization guideline for Hereditary Angioedema

Berinert, Cinryze, Firazyr, Haegarda, Kalbitor, Ruconest, Takhzryo

Prior Authorization Guidelines for All indications *(submission of medical records and labs are required)*:

A. The medication requested is used for the management of hereditary angioedema OR for the treatment of documented acute attacks of angioedema induced from angiotensin-converting enzyme (ACE) inhibitors *(Firazyr only)*; **AND**

B. Medication is being prescribed by an allergy and immunology specialist, hematologist, or dermatologist; **AND**

C. The diagnosis of hereditary angioedema is confirmed by laboratory values:
   1. Hereditary Angioedema Type I
      i. Low C4 level; **AND**
      ii. Low C1-INH antigenic level
   2. Hereditary Angioedema Type II
      i. Low C4 level; **AND**
      ii. Normal or elevated C1-INH antigenic level AND low C1-INH functional level
   3. Hereditary Angioedema Type III
      i. Normal C4 level; **AND**
      ii. Normal C1-INH antigenic level AND normal C1-INH functional level; **AND**
      iii. Documentation of a family history of hereditary angioedema or has a known hereditary angioedema (HAE)-causing mutation

D. There is a documented history of at least one symptom of a moderate to severe hereditary angioedema attack (e.g., moderate to severe abdominal pain, facial swelling, airway swelling) in the absence of hives or a medication known to cause angioedema; **AND**

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E. The member is not taking any medications that may exacerbate hereditary angioedema, including angiotensin-converting enzyme (ACE) inhibitors and estrogen-containing medications.

Additional criteria for acute treatment against hereditary angioedema when the following criteria are met (Berinert, Kalbitor, Ruconest, Firazyr):

A. The member’s age is appropriate for the specific medication requested (all age groups for Berinert, ≥ 18 years for Firazyr, ≥ 12 years for Kalbitor and Ruconest);

B. The requested medication is being used for the treatment of acute hereditary angioedema attacks, except the use of Ruconest for those with laryngeal attacks;

C. Firazyr will be used for the treatment of documented acute attacks of angioedema induced from angiotensin-converting enzyme (ACE) inhibitors.

D. Berinert, Firazyr, Kalbitor, or Ruconest will not be used together.

Additional criteria for prophylaxis against hereditary angioedema when the following criteria are met (Cinryze, Haegarda, Takhzyro):

A. The member’s age is appropriate for the specific medication requested (≥ 6 years for Cinryze, ≥ 12 years for Haegarda and Takhzyro); AND

B. The member has no signs of current acute angioedema; AND

C. Member has a history of at least one hereditary angioedema (HAE) attack per month; AND

D. Treatment with 17 alpha-alkylated androgens (e.g. danazol, stanozolol) or anti-fibrinolytic agents(e.g. epsilon aminocaproic acid, tranexamic acid) for hereditary angioedema prophylaxis was ineffective or not tolerated, or both classes of medications are contraindicated; AND

E. Cinryze, Takhzyro, and Haegarda will not be used together.

Initial Approval:
- Angiotensin-Converting Enzyme (ACE) Inhibitor Induced Angioedema: 3 doses
- All other indications: 3 months

Renewal:

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• Duration: 6 months
• Requires: Documentation demonstrating disease state improvement (e.g., a decrease in the number, severity, and/or duration of acute hereditary angioedema attacks) is provided

**Dosing and administration:**

<table>
<thead>
<tr>
<th>Medication</th>
<th>Maximum Dose</th>
<th>Available Dose</th>
<th>Quantity Limits</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cinryze</td>
<td>1,000 Units every 3 or 4 days*</td>
<td>500 units (lyophilized) in an 8 mL vial</td>
<td>Up to 20 vials per 28 days**</td>
</tr>
<tr>
<td>Haegarda</td>
<td>60 IU/kg twice weekly (every 3 or 4 days)</td>
<td>2,000 and 3,000 IU single-use vials</td>
<td>Up to 17 vials per 28 days or needed quantity based on weight provided for member**</td>
</tr>
<tr>
<td>Takhzyro</td>
<td>300 mg every 2 weeks</td>
<td>300 mg/2 mL (150 mg/mL) vial</td>
<td>Up to 2 vials per 28 days</td>
</tr>
</tbody>
</table>

*Doses up to 2,500 units (not exceeding 100 units/kg) every 3 or 4 days may be considered based on individual patient response

**Larger doses may be reviewed to determine medical necessity suggest sending to medical director for final review

**Additional information:**

**Laboratory Values:**

- **C4 levels:** low C4 level (C4 less than 14 mg/dL); normal C4 range (14 to 40 mg/dL), or C4 below the lower limit of normal as defined by the laboratory performing the test
- **C1INH antigenic level:** low C1INH (less than 19 mg/dL); normal range 19 to 37 mg/dL, or C1INH antigenic level below the lower limit of normal as defined by the laboratory performing the test;

**References:**

2. Berinert (C1 esterase inhibitor, human) [package insert]. CSL Behring LLC, Kankakee, IL; September 2017. Accessed July 6, 2018

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7. Drug Facts and Comparisons online. [Internet database], Wolters Kluwer Health, St. Louis, MO. Updated periodically


