

**Pharmacy Prior Authorization
Hereditary Angioedema – Clinical Guideline**

Berinert (human C1 esterase inhibitor), **Cinryze** (C1 esterase inhibitor), **Firazyr** (icatibant)

Kalbitor (ecallantide), **Ruconest** (recombinant C1 esterase inhibitor), **Takhzyro** (lanadelumab)

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

- The medication requested is used for the management of hereditary angioedema; **AND**
- Medication is being prescribed by an allergy and immunology specialist, hematologist, or dermatologist; **AND**
- The diagnosis of hereditary angioedema is confirmed by laboratory values:
 - Hereditary Angioedema Type I
 - Low C4 level; **AND**
 - Low C1-INH antigenic level
 - Hereditary Angioedema Type II
 - Low C4 level; **AND**
 - Normal or elevated C1-INH antigenic level AND low C1-INH functional level
 - Hereditary Angioedema Type III
 - Normal C4 level; **AND**
 - Normal C1-INH antigenic level AND normal C1-INH functional level; **AND**
 - Documentation of a family history of hereditary angioedema or has a known hereditary angioedema (HAE)-causing mutation
- 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**
- 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):

- 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);
- The requested medication is being used for the treatment of acute hereditary angioedema attacks, except the use of Ruconest for those with laryngeal attacks;
- Firazyr will be used for the treatment of documented acute attacks of angioedema induced from angiotensin-converting enzyme (ACE) inhibitors.
- 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):

- The member's age is appropriate for the specific medication requested (≥ 6 years for Cinryze, ≥ 12 years for Haegarda and Takhzyro); **AND**
- The member has no signs of current acute angioedema; **AND**
- Member has a history of at least one hereditary angioedema (HAE) attack per month; **AND**

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- 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**
- 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:

- 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
- Renewals not applicable to Angiotensin-Converting Enzyme (ACE) Inhibitor Induced Angioedema

Dosing and administration:

Medication	Maximum Dose	Available Dose	Quantity Limits
Cinryze	1,000 Units every 3 or 4 days	500 units (lyophilized) in an 8 mL vial	Up to 17 vials per 30 days**
Haegarda	60 IU/kg twice weekly (every 3 or 4 days)	2,000 and 3,000 IU single-use vials	Up to 17 vials per 30 days**
Takhzyro	300 mg every 2 weeks	300 mg/2 mL (150 mg/mL) vial	Up to 2 vials per 28 days

*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:

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