Pharmacy Prior Authorization
Hereditary Angioedema – Clinical Guideline

Berinert (human C1 esterase inhibitor)
Haegarda (human C1 esterase inhibitor)
Takhzyro (lanadelumab, kallikrein inhibitor)
Firazyr (icatibant, synthetic bradykinin B_2-receptor antagonist)
Cinryze (human C1 esterase inhibitor)
Ruconest (recombinant C1 esterase inhibitor)
Kalbitor (ecallantide, Kallikrein inhibitor)

Submission of Medical Records and Labs are Required for Both Initial and Renewal Requests

Prior Authorization Guidelines for All indications:

- Medication requested is used for management of hereditary angioedema
- Medication is being prescribed by an allergy and immunology specialist, hematologist, or dermatologist
- Diagnosis of hereditary angioedema is confirmed by laboratory values:
  - Hereditary Angioedema Type I
    - Low C4 level
    - Low C1-INH antigenic level
  - Hereditary Angioedema Type II
    - Low C4 level
    - Normal or elevated C1-INH antigenic level and low C1-INH functional level
  - Hereditary Angioedema Type III
    - No evidence of urticaria
    - Normal C4 level
    - Normal C1-INH antigenic level and normal C1-INH functional level
    - Documentation of a family history of angioedema, and failure to respond to chronic, high-dose antihistamine therapy, or a known hereditary angioedema) causing mutation
- Documented history of at least one symptom of a moderate to severe hereditary angioedema attack (for example moderate to severe abdominal pain, facial swelling, airway swelling) in the absence of hives, or a medication known to cause angioedema
- Member is not taking any medications that may exacerbate hereditary angioedema, including angiotensin-converting enzyme (ACE) inhibitors, or estrogen-containing medications

Additional Criteria:

Acute Treatment of Hereditary Angioedema (Berinert, Kalbitor, Ruconest, Firazyr):

- Member's age is appropriate for the specific medication requested (all age groups for Berinert, greater than or equal to 18 years for Firazyr, greater than or equal to 12 years for Kalbitor and Ruconest)
- Requested medication is being used for the treatment of an acute hereditary angioedema attack (Ruconest not proven effective for those with a laryngeal attack)
- Firazyr may be used for the treatment of a documented acute attack of angioedema induced due to use of an angiotensin-converting enzyme (ACE) inhibitor

Effective: 4/2020

- Berinert, Firazyr, Kalbitor, or Ruconest will not be used together

Additional Criteria for Prophylaxis Against Hereditary Angioedema (Cinryze, Haegarda, Takhzyro):

- Member's age is appropriate for the specific medication requested (greater than or equal to 6 years for Cinryze, greater than or equal to 12 years for Haegarda and Takhzyro)
- Member has no signs of current acute angioedema
- Member has a history of at least one hereditary angioedema attack per month
- Treatment with 17 alpha-alkylated androgens (for example danazol, stanozolol), or anti-fibrinolytic agents (for example epsilon aminocaproic acid, tranexamic acid) for hereditary angioedema prophylaxis was ineffective, or not tolerated, or both classes of medications are contraindicated
- Cinryze, Takhzyro, and Haegarda will not be used together

Initial Approval:

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

Renewal:

- Duration: 6 months

Requires:

- Documentation demonstrating disease state improvement (for example a decrease in number, severity, and/or duration of acute hereditary angioedema attacks) is provided
- Renewals are 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 and up to 1,000 units every 3 to 4 days in pediatric members 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 laboratory performing the test)

References:

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