Hereditary Angioedema (HAE) Therapies

**BENEFIT APPLICATION**

Benefit determinations are based on the applicable contract language in effect at the time the services were rendered. Exclusions, limitations or exceptions may apply. Benefits may vary based on contract, and individual member benefits must be verified. Wellmark determines medical necessity only if the benefit exists and no contract exclusions are applicable. This policy may not apply to FEP. Benefits are determined by the Federal Employee Program.

**DESCRIPTION**

The intent of the hereditary angioedema (HAE) therapies drug policy is to ensure appropriate selection of patients for therapy based on product labeling, clinical guidelines and clinical studies while steering utilization to the most cost-effective medication within the therapeutic class.

There are presently six (6) HAE therapies included in this policy: Berinert (C1 esterase inhibitor), Cinryze (C1 inhibitor), Firazyr (icatibant) a selective bradykinin B2 receptor antagonist, Haegarda (C1 inhibitor), Kalbitor (ecallantide) a selective, reversible kallikrien inhibitor and Ruconest (conestat alfa) a recombinant C1 esterase inhibitor. All HAE therapies inhibit either the formation or the activity of bradykinin, whose overproduction in the setting of C1 esterase inhibitor (C1INH) deficiency leads to capillary leakage and fluid accumulation in body tissues resulting in HAE symptoms. HAE therapies are administered by either intravenous (Ruconest, Berinert and Cinryze) or subcutaneous (Firazyr, Haegarda and Kalbitor) injection.

Ruconest is the preferred product for the treatment of acute attacks of hereditary angioedema. The criteria will require the use of the health plan’s preferred product Ruconest before the use of targeted product Berinert, unless there are clinical circumstances that exclude the use of the preferred product and may be based on previous use of a product.

**FDA-Approved Indication**

- **Berinert**: treatment of acute abdominal, facial, or laryngeal attacks of HAE in adult and pediatric patients
- **Cinryze**: routine prophylaxis against angioedema attacks in adolescent and adult patients with HAE
- **Haegarda**: routine prophylaxis against angioedema attacks in adolescent and adult patients with HAE
- **Firazyr**: treatment of acute attacks of HAE in adults 18 years of age and older
- **Kalbitor**: treatment of acute attacks of HAE in patients 12 years of age and older
- **Ruconest**: treatment of acute attacks in adults and adolescent patients with HAE

**Compendial Use**

- **Berinert**: prophylaxis of HAE attacks
- **Cinryze**: treatment of acute HAE attacks
CRITERIA FOR INITIAL APPROVAL

I. Berinert may be considered **medically necessary** for the prevention of HAE attacks when either of the following criteria is met:

- Member C1 inhibitor deficiency as confirmed by laboratory testing.
- Member has normal C1 inhibitor as confirmed by laboratory testing and meets one of the following criteria:
  - Member has an F12, angiopoietin-1, or plasminogen gene mutation as confirmed by genetic testing or
  - Member has a family history of angioedema and the angioedema was refractory to a trial of high-dose antihistamine (e.g., cetirizine) for at least one month.

Approval will be for **lifetime**.

II. Berinert may be considered **medically necessary** for the treatment of HAE attacks when the following criteria is met:

- Member must meet at least one of the following exception criteria:
  - Member is currently receiving treatment with Berinert through health insurance, excluding it is obtained as samples or via manufacturer’s patient assistance programs.
  - Member has tried and experienced an inadequate response to Ruconest.
  - Member has tried and experienced an intolerable adverse event to Ruconest.
  - Member has a contraindication to Ruconest (i.e., known or suspected allergy to rabbits or rabbit-derived products).
  - Member is less than 13 years of age.
  - Berinert is being requested for treatment of laryngeal attacks.

AND
- Member C1 inhibitor deficiency as confirmed by laboratory testing.

OR
- Member has normal C1 inhibitor as confirmed by laboratory testing and meets one of the following criteria:
  - Member has an F12, angiopoietin-1, or plasminogen gene mutation as confirmed by genetic testing or
  - Member has a family history of angioedema and the angioedema was refractory to a trial of high-dose antihistamine (e.g., cetirizine) for at least one month.

Approval will be for **lifetime**.

III. Cinryze may be considered **medically necessary** for the treatment and prevention of HAE attacks when either of the following criteria is met:

- Member C1 inhibitor deficiency as confirmed by laboratory testing.
- Member has normal C1 inhibitor as confirmed by laboratory testing and meets one of the following criteria:
  - Member has an F12, angiopoietin-1, or plasminogen gene mutation as confirmed by genetic testing or
  - Member has a family history of angioedema and the angioedema was refractory to a trial of high-dose antihistamine (e.g., cetirizine) for at least one month.

Approval will be for **lifetime**.
IV. Firazyr may be considered medically necessary for the treatment of acute HAE attacks in member 18 years of age or older when either of the following criteria is met:

- Member has C1 inhibitor deficiency as confirmed by laboratory testing.
- Member has normal C1 inhibitor as confirmed by laboratory testing and meets one of the following criteria:
  - Member has an F12, angiopoietin-1, or plasminogen gene mutation as confirmed by genetic testing.
  - Member has a family history of angioedema and the angioedema was refractory to a trial of high-dose antihistamine (e.g., cetirizine) for at least one month.

Approval will be for lifetime.

V. Haegarda may be considered medically necessary for the prevention of HAE attacks when either of the following criteria is met:

- Member C1 inhibitor deficiency as confirmed by laboratory testing.
- Member has normal C1 inhibitor as confirmed by laboratory testing and meets one of the following criteria:
  - Member has an F12, angiopoietin-1, or plasminogen gene mutation as confirmed by genetic testing, or
  - Member has a family history of angioedema and the angioedema was refractory to a trial of high-dose antihistamine (e.g., cetirizine) for at least one month.

Approval will be for lifetime.

VI. Kalbitor may be considered medically necessary for the treatment of acute HAE attacks in members 12 years of age or older when the following criteria is met:

- Member C1 inhibitor deficiency as confirmed by laboratory testing.
- Member has normal C1 inhibitor as confirmed by laboratory testing and meets one of the following criteria:
  - Member has an F12, angiopoietin-1, or plasminogen gene mutation as confirmed by genetic testing or
  - Member has a family history of angioedema and the angioedema was refractory to a trial of high-dose antihistamine (e.g., cetirizine) for at least one month.

Approval will be for lifetime.

VII. Ruconest may be considered medically necessary for the treatment of acute HAE attacks when the following criteria is met:

- Member C1 inhibitor deficiency as confirmed by laboratory testing.
- Member has normal C1 inhibitor as confirmed by laboratory testing and meets one of the following criteria:
  - Member has an F12, angiopoietin-1, or plasminogen gene mutation as confirmed by genetic testing or
  - Member has a family history of angioedema and the angioedema was refractory to a trial of high-dose antihistamine (e.g., cetirizine) for at least one month.

Approval will be for lifetime.

VIII. Berinert, Cinryze, Firazyr, Haegarda, Kalbitor and Ruconest are considered not medically necessary for patients who do not meet the criteria set forth above.
CONTINUATION OF THERAPY

I. All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

PROCEDURES AND BILLING CODES

To report provider services, use appropriate CPT* codes, Alpha Numeric (HCPCS level 2) codes, Revenue codes, and/or ICD diagnostic codes.

- J0596: Injection, C-1 esterase inhibitor (human), Ruconest, 10 units
- J0597: Injection, C-1 esterase inhibitor (human), Berinert, 10 units
- J0598: Injection, C-1 esterase inhibitor (human), Cinryze, 10 units
- J1290: Injection, ecallantide, Kalbitor, 1 mg
- J1744: Injection, icatibant, Firazyr, 1 mg
- C9445: Injection, C-1 esterase Inhibitor (recombinant), Ruconest, 10 units
- C9015: injection, C-1 esterase Inhibitor Subcutaneous (human), Haegarda
- J0599: injection, C-1 esterase Inhibitor Subcutaneous (human), Haegarda (effective 1.1.2019)
- J3490: unclassified drugs

REFERENCES


**POLICY HISTORY**

**Policy #:** 05.01.23  
**Policy Creation:** January 1, 2016  
**Reviewed:** January 2018  
**Revised:** January 2019  
**Current Effective Date:** January 2019