KAISER PERMANENTE - PORTLAND
MEDICATION REQUEST GUIDELINES

C1 ESTERASE INHIBITOR

<table>
<thead>
<tr>
<th>Generic</th>
<th>Brand</th>
<th>HICL</th>
<th>GCN</th>
<th>Exception/Other</th>
</tr>
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<tbody>
<tr>
<td>C1 ESTERASE INHIBITOR</td>
<td>BERINERT, CINRYZE</td>
<td>18568</td>
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<tr>
<td>C1 ESTERASE INHIBITOR, RECOMBINANT</td>
<td>RUCONEST</td>
<td>37766</td>
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GUIDELINES FOR USE

1. Does the patient have a diagnosis of hereditary angioedema (HAE) Type I or Type II as established by C1 inhibitor antigenic levels, C1 inhibitor functional levels AND C1q levels?
   - If yes, continue to #2.
   - If no, do not approve.
   **DENIAL TEXT:** See the denial text at the end of the guideline.

2. Is the medication being prescribed (or patient overseen) by a hematologist or allergy/immunologist?
   - If yes, continue to #3.
   - If no, do not approve.
   **DENIAL TEXT:** See the denial text at the end of the guideline.

3. Does the patient have documented frequent (at least 1 per month) or severe (causing disability for at least 5 days or history of airway compromise) HAE attacks?
   - If yes, continue to #4.
   - If no, do not approve.
   **DENIAL TEXT:** See the denial text at the end of the guideline.

4. Is the requested for C1 ESTERASE INHIBITOR (CINRYZE)?
   - If yes, continue to #5.
   - If no, approve for a duration of 12 months as follows:
     - BERINERT for up to 12 fills (each fill up to a maximum of #3 vials/kits)
     - RUCONEST for up to #4 vials per 30 days

5. Does the patient have documented contraindication, inadequate response or inability to tolerate adverse effects of 17α-alkylated androgens (e.g., danazol)?
   - If yes, approve for a duration of 12 months as follows:
     - BERINERT for up to 12 fills (each fill up to a maximum of #3 vials/kits)
     - RUCONEST for up to #4 vials per 30 days
   - If no, do not approve.
   **DENIAL TEXT:** See the denial text at the end of the guideline.

**DENIAL TEXT:** Approval requires a diagnosis of hereditary angioedema Type I or Type II; medication being prescribed or patient overseen by hematologist or immunologist; documented frequent or severe HAE attacks; and additionally for CINRYZE documented
contraindication, and inadequate response or inability to tolerate adverse effects of 17α-alkylated androgens (e.g., danazol).

CONTINUED ON NEXT PAGE
RATIONAL
To ensure the appropriate use of Berinert, Cinryze, and Ruconest in patients with hereditary angioedema (HAE).

FDA APPROVED INDICATIONS
Berinert:
- is a plasma-derived C1 esterase inhibitor (human) indicated for the treatment of acute abdominal, facial, or laryngeal attacks of hereditary angioedema in adult and adolescent patients.
- The safety and efficacy of Berinert for prophylactic therapy have not been established.

Cinryze:
- is a C1 inhibitor indicated for routine prophylaxis against angioedema in adolescent and adult patients with hereditary angioedema.

Ruconest:
- is indicated for the treatment of acute attacks in adult and adolescent patients with hereditary angioedema (HAE).
- Limitation of use: Effectiveness was not established in HAE patients with laryngeal attacks.

DOSAGE
Berinert
The dose is 20 International Units (IU) per kg body weight by intravenous injection. Doses lower than 20 IU/kg body weight should not be administered. Each Berinert vial containing 500 IU of C1 esterase inhibitor as a lyophilized concentrate for reconstitution with 10 mL of Sterile Water for Injection.

Cinryze
A dose of 1,000 Units can be administered every 3 or 4 days for routine prophylaxis against angioedema attacks in HAE patients. Cinryze is administered at an injection rate of 1 mL per minute. To obtain the required dose, reconstitute two Cinryze vials with two vials Sterile Water for Injection, USP (5 mL each) using aseptic sterile technique.

Ruconest
The dose is 50 IU/kg for patients less than 84 kg, or 4200 IU for patients that weigh 84 kg or more. Each vial (2100 IU) should be reconstituted by adding 14 mL of sterile water for injection to obtain a solution of 150 IU/mL. After reconstitution the dose can be administered as a slow intravenous injection over 5 minutes. If appropriately trained, patients may self-administer the dose as needed upon recognition of an HAE attack. No more than two doses should be administered within a 24-hour period, and no more than 4200 IU per dose should be administered.

REFERENCES