Medical Guideline Disclaimer

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I. Length of Authorization

Coverage will be provided for 12 months and may be renewed.

II. Dosing Limits

A. Max Units (per dose and over time) [Medical Benefit]:
   - 1,000 billable units per 30 days

III. Initial Approval Criteria

Prophylaxis against angioedema attacks of Hereditary Angioedema (HAE) †

- Must be prescribed by, or in consultation with, a specialist in: allergy, immunology, hematology, pulmonology, or medical genetics; AND
- Patient must be at least 6 years of age; AND
- Patient has a history of one of the following criteria for long-term HAE prophylaxis:
  - History of two (2) or more severe HAE attacks per month (i.e., airway swelling, debilitating cutaneous or gastrointestinal episodes); OR
  - Patient is disabled more than 5 days per month by HAE; OR
- History of at least one laryngeal attack caused by HAE; AND
- Treatment of patient with “on-demand” therapy (i.e., Kalbitor, Firazyr, Ruconest, or Berinert) did not provide satisfactory control or access to “on-demand therapy” is limited; AND
- Not used in combination with C1 inhibitor prophylaxis (e.g., Haegarda or Takhzyro); AND
- Confirmation the patient is avoiding the following possible triggers for HAE attacks:
  - Estrogen-containing oral contraceptive agents AND hormone replacement therapy; AND
  - Antihypertensive agents containing ACE inhibitors; AND
- Patient has one of the following clinical presentations consistent with HAE subtype, which must be confirmed by repeat blood testing:

### HAE I (C1-Inhibitor deficiency)
- Low C1 inhibitor (C1-INH) antigenic level (C1-INH antigenic level below the lower limit of normal as defined by the laboratory performing the test); AND
- Low C4 level (C4 below the lower limit of normal as defined by the laboratory performing the test); AND
- Low C1-INH functional level (C1-INH functional level below the lower limit of normal as defined by the laboratory performing the test); AND
  - Patient has a family history of HAE; OR
  - Onset of HAE symptoms occurred before age 30; OR
  - Normal C1q level

### HAE II (C1-Inhibitor dysfunction)
- Normal to elevated C1-INH antigenic level; AND
- Low C4 level (C4 below the lower limit of normal as defined by the laboratory performing the test); AND
- Low C1-INH functional level (C1-INH functional level below the lower limit of normal as defined by the laboratory performing the test)

### HAE with normal C1INH (formerly known as HAE III)
- Prophylaxis for HAE with normal C1-INH is not routinely recommended and will be evaluated on a case by case basis

† FDA Approved Indication(s)

### IV. Renewal Criteria
- Patient continues to meet the criteria in section III; AND
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include the following: severe hypersensitivity reactions, serious thrombotic events, laryngeal attacks, etc.; AND
o Significant improvement in severity and duration of attacks have been achieved and sustained; OR
o Patient requires dose titration due to an inadequate response to therapy (> 1.0 HAE attack/month, regardless of severity/duration)

V. Dosage/Administration

<table>
<thead>
<tr>
<th>Indication</th>
<th>Dose</th>
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<tbody>
<tr>
<td><strong>Hereditary Angioedema (HAE)</strong></td>
<td><strong>Adult/adolescents (≥12 years old)</strong> 1,000 units by intravenous injection every 3 to 4 days</td>
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<td></td>
<td>For patients who have not responded adequately to initial dosing, doses up to 2,500 U (not exceeding 100 U/kg) every 3 or 4 days may be considered based on individual patient response.</td>
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<tr>
<td></td>
<td><strong>Pediatric patients (6 to 11 years old)</strong> 500 units by intravenous injection every 3 to 4 days</td>
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<tr>
<td></td>
<td>The dose may be adjusted according to individual patient response, up to 1,000 U every 3 to 4 days.</td>
</tr>
</tbody>
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Limitations/Exclusions
Cinryze® (C1 Esterase Inhibitor Human) is not considered medically necessary for indications other than those listed above due to insufficient evidence of therapeutic value.

Applicable Procedure Codes

<table>
<thead>
<tr>
<th>Procedure Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>J0598</td>
<td>Injection, C1 esterase inhibitor (human), Cinryze, 10 units</td>
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</tbody>
</table>

Applicable NDCs

<table>
<thead>
<tr>
<th>NDC Code</th>
<th>Description</th>
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<tbody>
<tr>
<td>42227-0081-xx</td>
<td>Cinryze 500 units single-dose vial</td>
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Applicable Diagnosis Codes

<table>
<thead>
<tr>
<th>Diagnosis Code</th>
<th>Description</th>
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<tbody>
<tr>
<td>D84.1</td>
<td>Defects in the complement system</td>
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Revision History

N/A
VI. References


