Cinryze® (C1 Esterase Inhibitor Human)  
(Intravenous)  

Document Number: IC-0168  

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 9 years of age; AND  
- Patient has a history of one of the following criteria for long-term HAE prophylaxis:  
  o History of two (2) or more severe HAE attacks per month (i.e., airway swelling, debilitating cutaneous or gastrointestinal episodes); OR  
  o Patient is disabled more than 5 days per month by HAE; OR  
  o History of recurrent laryngeal attacks 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  
- Patient has tried and failed, is intolerant, or has a contraindication to attenuated (17 alpha-alkylated) androgens (i.e., danazol) for HAE prophylaxis; AND  
- Confirmation the patient is avoiding the following possible triggers for HAE attacks:  
  o Helicobacter pylori infections (confirmed by lab test)  
  o Estrogen-containing oral contraceptive agents OR hormone replacement therapy  
  o Antihypertensive agents containing ACE inhibitors; AND
• Patient has one of the following clinical presentations consistent with HAE subtype:

### HAE I
- 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**
  - Normal C1q level

### HAE II
- 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)
- Normal C1-INH antigenic level: **AND**
- Normal C4 level: **AND**
- Normal C1-INH functional level: **AND**
  - Patient has a known HAE-causing C1-INH mutation (i.e., mutation of coagulation factor XII gene [F12 mutation]): **OR**
  - Patient has a family history of HAE and documented evidence of lack of efficacy of chronic high-dose antihistamine therapy (e.g. cetirizine standard dosing at up to four times daily or an alternative equivalent, given for at least one month or an interval long enough to expect three or more angioedema attacks)

† 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: severe hypersensitivity reactions, serious thrombotic events, laryngeal attacks, etc.: **AND**
  - Significant improvement in severity and duration of attacks have been achieved and sustained: **OR**
  - 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>
</tr>
</thead>
<tbody>
<tr>
<td>Hereditary Angioedema (HAE)</td>
<td>1,000 units by intravenous injection every 3 to 4 days</td>
</tr>
<tr>
<td></td>
<td>For patients who have not responded adequately to initial dosing,</td>
</tr>
<tr>
<td></td>
<td>doses up to 2,500 U (not exceeding 100 U/kg) every 3 or 4 days</td>
</tr>
<tr>
<td></td>
<td>may be considered based on individual patient response.</td>
</tr>
</tbody>
</table>

VI. Billing Code/Availability Information

Jcode:

- J0598 – Injection, C1 esterase inhibitor (human), Cinryze, 10 units: 1 billable unit = 10 units
- NDC:
  - Cinryze 500 mg single-dose vial: 42227-0081-xx

VII. References


Appendix 1 – Covered Diagnosis Codes

<table>
<thead>
<tr>
<th>ICD-10</th>
<th>ICD-10 Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>D84.1</td>
<td>Defects in the complement system</td>
</tr>
</tbody>
</table>

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determination (NCD) and Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. They can be found at: http://www.cms.gov/medicare-coverage-database/search/advanced-search.aspx. Additional indications may be covered at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCD): N/A

<table>
<thead>
<tr>
<th>Jurisdiction</th>
<th>Applicable State/US Territory</th>
<th>Contractor</th>
</tr>
</thead>
<tbody>
<tr>
<td>E (1)</td>
<td>CA, HI, NV, AS, GU, CNMI</td>
<td>Noridian Healthcare Solutions, LLC</td>
</tr>
<tr>
<td>F (2 &amp; 3)</td>
<td>AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ</td>
<td>Noridian Healthcare Solutions, LLC</td>
</tr>
<tr>
<td>5</td>
<td>KS, NE, IA, MO</td>
<td>Wisconsin Physicians Service Insurance Corp</td>
</tr>
<tr>
<td>6</td>
<td>MN, WI, IL</td>
<td>National Government Services, Inc. (NGS)</td>
</tr>
<tr>
<td>H (4 &amp; 7)</td>
<td>LA, AR, MS, TX, OK, CO, NM</td>
<td>Novitas Solutions, Inc.</td>
</tr>
<tr>
<td>8</td>
<td>MI, IN</td>
<td>Wisconsin Physicians Service Insurance Corp</td>
</tr>
<tr>
<td>N (9)</td>
<td>FL, PR, VI</td>
<td>First Coast Service Options, Inc.</td>
</tr>
<tr>
<td>J (10)</td>
<td>TN, GA, AL</td>
<td>Palmetto Government Benefit Administrators, LLC</td>
</tr>
<tr>
<td>M (11)</td>
<td>NC, SC, WV, VA (excluding below)</td>
<td>Palmetto GBA, LLC</td>
</tr>
<tr>
<td>L (12)</td>
<td>DE, MD, PA, NJ, DC (includes Arlington &amp; Fairfax counties and the city of Alexandria in VA)</td>
<td>Novitas Solutions, Inc.</td>
</tr>
<tr>
<td>K (13 &amp; 14)</td>
<td>NY, CT, MA, RI, VT, ME, NH</td>
<td>National Government Services, Inc. (NGS)</td>
</tr>
<tr>
<td>15</td>
<td>KY, OH</td>
<td>CGS Administrators, LLC</td>
</tr>
</tbody>
</table>