Berinert® (C1 Esterase Inhibitor, Human) (Intravenous)

I. Length of Authorization

Coverage will be provided for 12 weeks and is eligible for renewal.

The cumulative amount of medication(s) the patient has on-hand, indicated for the acute treatment of HAE, will be taken into account when authorizing. The authorization will provide a sufficient quantity in order for the patient to have a cumulative amount of HAE medication(s) on-hand in order to treat up to 4 acute attacks per 4 weeks for the duration of the authorization.

II. Dosing Limits

A. Quantity Limit (max daily dose) [Pharmacy Benefit]:
   - Berinert 500 IU vial: 22 vials every 28 days

B. Max Units (per dose and over time) [Medical Benefit]:
   - 1100 billable units per 28 days

III. Initial Approval Criteria

Treatment of acute abdominal, facial, or laryngeal 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
- 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 a history of moderate to severe cutaneous attacks (without concomitant hives) OR abdominal attacks OR mild to severe airway swelling attacks of HAE (i.e. debilitating cutaneous/gastrointestinal symptoms OR laryngeal/pharyngeal/tongue swelling); 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**
  - Acquired angioedema has been ruled out (i.e., patient onset of symptoms occur prior to 30 years old, normal C1q levels, patient does not have underlying disease such as lymphoma or benign monoclonal gammopathy [MGUS], etc.)

**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 (also known as HAE III)**

- Normal C1-INH antigenic level: **AND**
- Normal C4 level: **AND**
- Normal C1-INH functional level: **AND**
- Repeat blood testing during an attack has confirmed the patient does not have abnormal lab values indicative of HAE I or HAE II: **AND**
- Either of the following:
  - Patient has a known HAE-causing mutation (e.g., mutation of coagulation factor XII gene [F12 mutation], mutation in the angiopoietin-1 gene, mutation in the plasminogen gene, etc.): **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): **AND** corticosteroids

† FDA Approved Indication(s)

**IV. Renewal Criteria**

- Patient continues to meet the criteria in section III: **AND**
- Significant improvement in severity and duration of attacks have been achieved and sustained: **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include the following: hypersensitivity reactions, serious thrombotic events (arterial or venous), laryngeal HAE attacks, etc.: **AND**
- The cumulative amount of medication(s) the patient has on-hand, indicated for the acute treatment of HAE, will be taken into account when authorizing. The authorization will provide a sufficient quantity in order for the patient to have a cumulative amount of HAE medication(s) on-hand in order to treat up to 4 acute attacks per 4 weeks for the duration of the authorization.
V. Dosage/Administration

<table>
<thead>
<tr>
<th>Indication</th>
<th>Dose</th>
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<tr>
<td>Acute Hereditary Angioedema (HAE) attack</td>
<td>20 international units (IU) per kg body weight by intravenous injection upon recognition of an HAE attack.</td>
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</tbody>
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VI. Billing Code/Availability Information

Jcode:
- J0597 – Injection, C-1 esterase inhibitor (human), Berinert, 10 units; 1 billable unit = 10 units

NDC:
- Berinert 500 IU single-use vial: 63833-0825-xx

VII. References


Appendix 1 – Covered Diagnosis Codes

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

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<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>
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<tr>
<td>5</td>
<td>KS, NE, IA, MO</td>
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<tr>
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<td>MN, WI, IL</td>
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<td>8</td>
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<td>Novitas Solutions, Inc.</td>
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