Cinryze® (C1 Esterase Inhibitor Human)
(Intravenous)

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I. Length of Authorization

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

II. Dosing Limits

A. Quantity Limit (max daily dose) [NDC unit]:

- Cinryze 500 unit vial: 20 vials per 30 days

B. Max Units (per dose and over time) [HCPCS Unit]:

- 1,000 billable units per 30 days

III. Initial Approval Criteria[1-15]

Coverage is provided in the following conditions:

Universal Criteria:

- Must be prescribed by, or in consultation with, a specialist in: allergy, immunology, hematology, pulmonology, or medical genetics; **AND**
- Not used in combination with other prophylactic therapies targeting C1 inhibitor or kallikrein (i.e., 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**

Prophylaxis against angioedema attacks of Hereditary Angioedema (HAE) †

- 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**
- Patient has one of the following clinical presentations consistent with a 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** o Patient has a family history of HAE; **OR** o 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 (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 o Prior to consideration of long-term prophylaxis, the patient must have demonstrated: ▪ An inadequate response or intolerance to an adequate trial of prophylactic therapy with an antifibrinolytic agent (e.g., tranexamic acid (TXA) or aminocaproic acid) and/or a 17α-alkylated androgen (e.g., danazol) unless contraindicated. Female patients may derive additional benefit from progestins[16,17,18]; **AND** ▪ Response to therapy from an agent indicated for the treatment of acute attacks (i.e., C1 esterase inhibitor, icatibant, ecallantide, etc.)

† FDA Approved Indication(s)

IV. Renewal Criteria[1]

Coverage can be renewed based upon the following criteria:

- Patient continues to meet the universal criteria identified 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**

- 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

Indication	Dose
Prophylaxis of Hereditary Angioedema (HAE) attacks	**Adult/adolescents (≥12 years old)** 1,000 units by intravenous injection every 3 to 4 days – *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.* **Pediatric patients (6 to 11 years old)** 500 units by intravenous injection every 3 to 4 days – *The dose may be adjusted according to individual patient response, up to 1,000 U every 3 to 4 days.*

VI. Billing Code/Availability Information

Jcode:

- J0598 – Injection, C1 esterase inhibitor (human), Cinryze, 10 units; 1 billable unit = 10 units

NDC:

- Cinryze 500 units single-dose vial: 42227-0081-xx

VII. References

1. Cinryze [package insert]. Exton, PA; ViroPharma Biologics, Inc; June 2018. Accessed January 2020.
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Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
D84.1	Defects in the complement system

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

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