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 single-dose vial: 50 vials per 30 days

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

- 2,500 billable units per 30 days

III. Initial Approval Criteria [1]

Coverage is provided in the following conditions:

- For patients 12 years of age and older, patient must have tried and failed to respond to treatment with Takhzyro™ (lanadelumab-flyo) or a contraindication exists; **AND**

- Patient is at least 6 years of age; **AND**

Universal Criteria [1,13,20]

- 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 (i.e., Haegarda, etc.) or kallikrein (i.e., Takhzyro, Orladeyo, etc.); **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**
  - Dipeptidyl peptidase IV (DPP-IV) inhibitors (e.g., sitagliptin); **AND**

- Neprilysin inhibitors (e.g., sacubitril); **AND**

Prophylaxis against angioedema attacks of Hereditary Angioedema (HAE) † Φ [1,13,20,21,22]

- Patient has one of the clinical presentations listed below consistent with an HAE subtype§, which must be confirmed by repeat blood testing (treatment for acute attack should not be delayed for confirmatory testing); **AND**
  - Patient is receiving treatment as short-term HAE prophylaxis prior to a procedure (i.e. dental or medical procedure); **OR**
  - 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)
    - Patient is disabled more than 5 days per month by HAE
    - 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

HAE I (C1-Inhibitor deficiency) § [13,20,21,22]
• 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) § [20,22]
• 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) § [20,21,22]
• 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[15,16,17]; **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); Φ Orphan Drug

IV. Renewal Criteria [1,13,20,21,22]

Coverage can be renewed based upon the following criteria:

- Patient continues to meet the universal and other indication-specific relevant criteria identified in section III; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: severe hypersensitivity reactions, serious thromboembolic events (arterial and venous), etc.; **AND**
  - Significant improvement in severity, frequency, and/or 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 [1]

Indication	Dose
Prophylaxis of Hereditary Angioedema (HAE) attacks	<u>Adult/adolescents (at least 12 years of age)</u> Administer 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.* <u>Pediatric patients (6 to 11 years of age)</u> Administer 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.* ***Note:** Patients may self-administer Cinryze after being instructed by their healthcare provider.*

VI. Billing Code/Availability Information

<u>HCPCS Code:</u>

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

<u>NDC:</u>

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

VII. References

1. Cinryze [package insert]. Exton, PA; ViroPharma Biologics, Inc; January 2021. Accessed August 2022.

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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), Local Coverage Determinations (LCDs), and Local Coverage Articles (LCAs) may exist and compliance with these policies is required where applicable. They can be found at: https://www.cms.gov/medicare-coverage-database/ 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/LCA): 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

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
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