Ruconest® (C1 Esterase Inhibitor [recombinant])
(Intravenous)

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I. Length of Authorization

- Initial*: Prior authorization validity will be provided initially for 12 weeks.
- Renewal*: Prior authorization validity may be renewed every 12 weeks thereafter.

*The cumulative amount of medication(s) the member 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 member 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

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

- 3360 billable units per 28 days

III. Initial Approval Criteria [1,22-24]

Prior authorization validity is provided in the following conditions:

- Member is at least 13 years of age; **AND**

Universal Criteria

- Must be prescribed by, or in consultation with, a specialist in allergy, immunology, hematology, pulmonology, or medical genetics; **AND**
- Member does NOT have any FDA labeled contraindications to the requested agent (e.g., known or suspected allergy to rabbits and rabbit-derived products, history of immediate hypersensitivity reactions, including anaphylaxis, to C1 esterase inhibitor preparations); **AND**
- Will not be used in combination with another agent indicated for the treatment of acute hereditary angioedema (HAE) attacks; ***NOTE****: Requests for combination duplicate therapy may be appropriate in some situations and will be reviewed on a case-by-case basis*; **AND**
- Provider will confirm member has been counseled to avoid possible medication triggers for HAE attacks (e.g. estrogen-containing medications, ACE inhibitors, etc.); **AND**

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Treatment of acute attacks of Hereditary Angioedema (HAE) † ‡ Φ

- Member has a history of ANY of the following:
  - Recurrent swelling of mucous membranes, skin surface, or subcutaneous tissue
  - Recurrent abdominal attacks with any of the following: severe abdominal pain, nausea, vomiting, or diarrhea
  - Episodes of upper airway (e.g., mouth, tongue, larynx, etc.) edema
  - Prodromal signs and symptoms (e.g., anxiety, nausea, paresthesia, fatigue, etc.) preceding angioedema attacks
  - Positive family history of HAE; **AND**
- Other causes of angioedema have been ruled out (e.g., drug-induced angioedema, mast cell-mediated angioedema, acquired angioedema due to C1-INH deficiency, etc.); **AND**
- Diagnosis of HAE has been confirmed as one of the following:
  - Member has HAE due to C1 inhibitor deficiency (HAE-C1-INH) Type 1 or 2; **AND**
    - Member has a current or historical C1-INH antigenic level below the lower limit of normal as defined by the laboratory performing the test; **OR**
    - Member has a current or historical C1-INH functional level below the lower limit of normal as defined by the laboratory performing the test; **OR**
    - Genetic testing confirming pathogenic mutation(s) in *SERPING1;* **OR**
  - Member has HAE with normal C1INH (HAE-nC1-INH); **AND**
    - Member has a current or historical normal C1-INH level (e.g., C1-INH antigenic level, C1-INH functional level) as defined by the laboratory performing the test; **AND**
      - Member has a confirmed presence of known HAE-causing mutation(s) in the gene(s) for factor XII (*F12),* angiopoietin-1 *(ANGPT1),* plasminogen *(PLG),* kininogen-1 *(KNG1),* myoferlin *(MYOF)*, and/or heparan sulfate-glucosamine 3-O-sulfotransferase 6 (*HS3ST6)*; **OR**
      - Member has recurrent angioedema attacks without hives that are refractory to a 4-week trial of high-dose antihistamines (i.e. second-generation H1 antagonist at four times the standard dose)

† FDA Approved Indication(s); **‡** Compendia Recommended Indication(s); **Φ** Orphan Drug

IV. Renewal Criteria [1,22-24]

Prior authorization validity can be renewed based upon the following criteria:

- Member continues to meet the universal and other indication-specific relevant criteria identified in section III; **AND**
- The member has experienced clinical benefit from therapy (e.g., reduced attack severity, shortened attack duration, etc.); **AND**

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- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: severe hypersensitivity reactions (including anaphylaxis), serious thromboembolic events (arterial or venous), etc.; **AND**
- The cumulative amount of medication(s) the member 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 member 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 [1]

Indication	Dose
Treatment of Acute Hereditary Angioedema (HAE) attack	Body weight < 84 kg: Administer 50 U per kg body weight by intravenous injection Body weight ≥ 84 kg: Administer 4200 U (2 vials) by intravenous injection *If the attack symptoms persist, an additional (second) dose can be administered at the recommended dose level. Do not exceed 4200 U per dose. No more than two doses should be administered within a 24-hour period.* ***Note:** Members may self-administer Ruconest upon recognition of symptoms of an HAE attack after being instructed by their healthcare provider.*

VI. Billing Code/Availability Information

HCPCS Code:

- J0596 - Injection, c1 esterase inhibitor (recombinant), ruconest, 10 units; 1 billable unit = 10 units

NDC:

- Ruconest 2100 U single-use 25 mL vial: 71274-0350-xx

VII. References

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Appendix A – Non-Quantitative Treatment Limitations (NQTL) Factor Checklist

Non-quantitative treatment limitations (NQTLs) refer to the methods, guidelines, standards of evidence, or other conditions that can restrict how long or to what extent benefits are provided under a health plan. These may include things like utilization review or prior authorization. The utilization management NQTL applies comparably, and not more stringently, to mental health/substance use disorder (MH/SUD) Medical Benefit Prescription Drugs and medical/surgical (M/S) Medical Benefit Prescription Drugs. The table below lists the factors that were considered in designing and applying prior authorization to this drug/drug group, and a summary of the conclusions that Prime's assessment led to for each.

Factor	Conclusion
Indication	Yes: Consider for PA
Safety and efficacy	No: PA not a priority
Potential for misuse/abuse	No: PA not a priority
Cost of drug	Yes: Consider for PA

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)

The preceding information is intended for non-Medicare coverage determinations. 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 Determinations (NCDs) and/or Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. Local Coverage Articles (LCAs) may also exist for claims payment purposes or to clarify

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benefit eligibility under Part B for drugs which may be self-administered. The following link may be used to search for NCD, LCD, or LCA documents: https://www.cms.gov/medicare-coverage-database/search.aspx. Additional indications, including any preceding information, may be applied 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 (WPS)
6	MN, WI, IL	Wellpoint Federal
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto GBA
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA
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	Wellpoint Federal
15	KY, OH	CGS Administrators, LLC

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