

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

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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]:

- Ruconest 2100 IU vial: 16 vials every 28 days

B. Max Units (per dose and over time) [Medical Benefit]:

- 3360 billable units per 28 days

III. Initial Approval Criteria

Treatment of acute abdominal, peripheral or facial 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 13 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)
<ul style="list-style-type: none"> • 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 <ul style="list-style-type: none"> ○ Patient has a family history of HAE; OR ○ Onset of HAE symptoms occurred before age 30; OR ○ Normal C1q level
HAE II (C1-Inhibitor dysfunction)
<ul style="list-style-type: none"> • 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)
<ul style="list-style-type: none"> • Normal C1-INH antigenic level; AND • Normal C4 level; AND • Normal C1-INH functional level; AND • Repeat blood testing <u>during an attack</u> has confirmed the patient does not have abnormal lab values indicative of HAE I or HAE II; AND • Either of the following: <ul style="list-style-type: none"> ○ 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 (<i>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</i>) 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, laryngeal 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

Indication	Dose
Acute Hereditary Angioedema (HAE) attack	<p><u>Body weight < 84 kg:</u> 50 international units (IU) per kg body weight by intravenous injection</p> <p><u>Body weight ≥ 84 kg:</u> 4200 IU (2 vials) by intravenous injection</p> <p><i>If the attack symptoms persist, an additional (second) dose can be administered at the recommended dose level. Do not exceed 4200 IU per dose. No more than two doses should be administered within a 24 hour period.</i></p>

VI. Billing Code/Availability Information

Jcode:

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

NDC:

- Ruconest 2100 IU single-use 25 mL vial: 68012-0350-xx

VII. References

1. Ruconest [package insert]. Raleigh, NC; Salix Pharmaceuticals, Inc; March 2018. Accessed August 2018.
2. Bygum A, Andersen KE, Mikkelsen CS. Self-administration of intravenous C1-inhibitor therapy for hereditary angioedema and associated quality of life benefits. *Eur J Dermatol.* Mar-Apr 2009;19(2):147-151.
3. Bowen T, Cicardi M, Farkas H, et al. 2010 International consensus algorithm for the diagnosis, therapy and management of hereditary angioedema. *Allergy Asthma Clin Immunol.* 2010;6(1):24.
4. Craig T, Aygören-Pürsün E, Bork K, et al. WAO Guideline for the Management of Hereditary Angioedema. *World Allergy Organ J.* 2012 Dec;5(12):182-99.
5. Gompels MM, Lock RJ, Abinun M, et al. C1 inhibitor deficiency: consensus document. *Clin Exp Immunol.* 2005;139(3):379.
6. Bowen T, Cicardi M, Farkas H, et al. Canadian 2003 International Consensus Algorithm For the Diagnosis, Therapy, and Management of Hereditary Angioedema. *J Allergy Clin Immunol.* 2004 Sep;114(3):629-37.
7. Betschel S, Badiou J, Binkley K, et al. Canadian hereditary angioedema guideline. *Asthma Clin Immunol.* 2014 Oct 24;10(1):50. doi: 10.1186/1710-1492-10-50.

8. Zuraw BL, Bernstein JA, Lang DM, et al. A focused parameter update: hereditary angioedema, acquired C1 inhibitor deficiency, and angiotensin-converting enzyme inhibitor-associated angioedema. *J Allergy Clin Immunol*. 2013 Jun;131(6):1491-3. doi: 10.1016/j.jaci.2013.03.034.
9. Zuraw BL, Banerji A, Bernstein JA, et al. US Hereditary Angioedema Association Medical Advisory Board 2013 recommendations for the management of hereditary angioedema due to C1 inhibitor deficiency. *J Allergy Clin Immunol Pract*. 2013 Sep-Oct;1(5):458-67.
10. Frank MM, Zuraw B, Banerji A, et al. Management of children with Hereditary Angioedema due to C1 Inhibitor deficiency. *Pediatrics*. 2016 Nov. 135(5)
11. Maurer M, Mager M, Ansotegui I, et al. The international WAO/EAACI guideline for the management of hereditary angioedema-The 2017 revision and update. *Allergy*. 2018 Jan 10. doi: 10.1111/all.13384.

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 (WPS)
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 (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto GBA, LLC
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA, LLC

Medicare Part B Administrative Contractor (MAC) Jurisdictions

Jurisdiction	Applicable State/US Territory	Contractor
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