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

Document Number: EOCCO-0207

Last Review Date: 08/01/2024
Date of Origin: 08/26/2014
Dates Reviewed: 03/2015, 06/2015, 09/2015, 12/2015, 03/2016, 06/2016, 09/2016, 12/2016, 03/2017, 06/2017, 09/2017, 12/2017, 03/2018, 06/2018, 10/2018, 10/2019, 03/2020, 10/2020, 10/2021, 10/2022, 10/2023, 08/2024

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) [NDC Unit]:

- Ruconest 2100 U single-use vial: 16 vials every 28 days

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

- 3360 billable units per 28 days

III. Initial Approval Criteria [1]

Coverage is provided in the following conditions:

- Patient has had a documented trial with inadequate response, intolerance or contraindication to the use of generic icatibant; **OR**
- Patient is less than 18 years of age

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

Universal Criteria [1,13,19]

- Must be prescribed by, or in consultation with, a specialist in allergy, immunology, hematology, pulmonology, or medical genetics; **AND**
- Patient does not have a history of allergy to rabbits or rabbit-derived products; **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 or angiotensin II receptor blockers (ARBs); **AND**
- Dipeptidyl peptidase IV (DPP-IV) inhibitors (e.g., sitagliptin); **AND**
- Neprilysin inhibitors (e.g., sacubitril); **AND**

Treatment of acute attacks of Hereditary Angioedema (HAE) † Φ [1,13,19,20,21]

- 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 a HAE subtype**§**, which must be confirmed by repeat blood testing (treatment for acute attack should not be delayed for confirmatory testing):

HAE I (C1-Inhibitor deficiency) §[13,19,20,21]
• 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 of age, normal C1q levels, patient does not have underlying disease such as lymphoma or benign monoclonal gammopathy [MGUS], etc.)
HAE II (C1-Inhibitor dysfunction) §[19,21]
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)

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

IV. Renewal Criteria [1]

- Patient continues to meet the universal and other indication-specific relevant criteria identified 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: severe hypersensitivity reactions (including anaphylaxis), serious thromboembolic events (arterial or venous), 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 [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:** Patients 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

1. Ruconest [package insert]. Warren, NJ; Pharming Healthcare, Inc; April 2020. Accessed July 2024.
2. Riedl MA, Grivcheva-Panovska V, Moldovan D, et al. Recombinant human C1 esterase inhibitor for prophylaxis of hereditary angio-oedema: a phase 2, multicentre, randomised, double-blind, placebo-controlled crossover trial. Lancet. 2017;390(10102):1595-1602.
3. 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.

4. 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.
5. 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.
6. 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.
7. Gompels MM, Lock RJ, Abinun M, et al. C1 inhibitor deficiency: consensus document. Clin Exp Immunol. 2005;139(3):379.
8. 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.
9. 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.
10. 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.
11. Frank MM, Zuraw B, Banerji A, et al. Management of children with Hereditary Angioedema due to C1 Inhibitor deficiency. Pediatrics. 2016 Nov. 135(5)
12. Zuraw BL, Bork K, Binkley KE, et al. Hereditary angioedema with normal C1 inhibitor function: Consensus of an international expert panel. Allergy Asthma Proc. 2012;33 Suppl 1:145-156.
13. 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.
14. Lang DM, Aberer W, Bernstein JA, et al. International consensus on hereditary and acquired angioedema. Ann Allergy Asthma Immunol. 2012;109:395-402.
15. Wintenberger C, Boccon-Gibod I, Launay D, et al. Tranexamic acid as maintenance treatment for non-histaminergic angioedema: analysis of efficacy and safety in 37 patients. Clin Exp Immunol. 2014 Oct; 178(1): 112–117.
16. Saule C, Boccon-Gibod I, Fain O, et al. Benefits of progestin contraception in non-allergic angioedema. Clin Exp Allergy. 2013 Apr;43(4):475-82.
17. Frank MM, Sergent JS, Kane MA, et al. Epsilon aminocaproic acid therapy of hereditary angioneurotic edema; a double-blind study. N Engl J Med. 1972:286:808-812.
18. Riedl MA, Bernstein JA, Li H, et al. Recombinant human C1-esterase inhibitor relieves symptoms of hereditary angioedema attacks: phase 3, randomized, placebo-controlled trial. Ann Allergy Asthma Immunol. 2014;112(2):163-169.e1.

19. Betschel S, Badiou J, Binkley K, et al. The International/Canadian Hereditary Angioedema Guideline. Allergy Asthma Clin Immunol. 2019; 15: 72. Published online 2019 Nov 25. doi: 10.1186/s13223-019-0376-8.
20. Busse PJ, Christiansen SC, Riedl MA, et al. US HAEA Medical Advisory Board 2020 Guidelines for the Management of Hereditary Angioedema. J Allergy Clin Immunol Pract. 2021 Jan;9(1):132-150.e3. doi: 10.1016/j.jaip.2020.08.046.
21. Maurer M, Magerl M, Betschel S, et al. The international WAO/EAACI guideline for the management of hereditary angioedema – The 2021 revision and update. Allergy. 2021 Nov 22. doi: 10.1111/all.15214

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 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	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
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.

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC