C1 esterase inhibitor [recombinant] (Ruconest®)	Place of Service Home infusion Administration Infusion Center Administration Office Administration Outpatient Facility Administration Self-Administration *(covered under Medical Benefit)* HCPCS: **J0596** per 10 units

Conditions listed in policy *(see criteria for details)*:

- Hereditary angioedema, treatment

AHFS therapeutic class: Complement inhibitor

Mechanism of action: Recombinant analogue of human complement component 1 esterase inhibitor. C1 inhibitor therapy in patients with C1 deficiency is believed to suppress contact system activation via inactivation of plasma kallikrein and factor XIIa, preventing bradykinin angioedema.

(1) Special Instructions and Pertinent Information

Covered under the medical benefit, please submit clinical information for prior authorization review via fax.

(2) Prior Authorization/Medical Review is required for the following condition(s)

All requests for Ruconest® for conditions NOT listed in section 3 must be sent for clinical review and receive authorization prior to drug administration or claim payment.

(3) The following condition(s) DO NOT require Prior Authorization/Preservice

All requests for Ruconest® for conditions NOT listed in section 3 must be sent for clinical review and receive authorization prior to drug administration or claim payment.

Hereditary angioedema (HAE), treatment

- Being used to treat acute attacks of hereditary angioedema (HAE)

Covered Doses
Up to 50 units/kg, max of 4200 units IV per dose, not to exceed 2 doses within a 24-hour period

Coverage Period
Cover once per attack

ICD-10:
D84.1

(4) This Medication is NOT medically necessary for the following condition(s)

Coverage for a Non-FDA approved indication, requires that criteria outlined in Health and Safety Code § 1367.21, including objective evidence of efficacy and safety are met for the proposed indication.

Please refer to the Provider Manual and User Guide for more information.

(5) Additional Information

How supplied:

- 2100 IU lyophilized powder for reconstitution for injection in a single-use vial

HAE Diagnosis[1]:

- Suspicion of HAE-1/2 should prompt laboratory investigations to support a diagnosis
    - Measurements of serum/plasma levels of C1-INH function, C1- INH protein, and C4 are used to diagnose HAE-1/2
    - HAE-1: Both concentration and function of C1-INH are low (<50% of normal).
    - HAE-2:
        - C1-INH concentrations are normal or elevated
        - C1-INH function is low (<50% of normal)
    - C4 levels are usually low in HAE-1/2 patients, but the sensitivity and specificity of C4 as a marker for HAE are limited.
    - Sequencing of the SERPING1 gene can be supportive in the diagnostic workup of some HAE-1/2 patients (including prenatal diagnosis); however, bio-chemical C1-INH testing is effective and less expensive than genetic testing
- HAE with normal C1 inhibitor (HAE-nC1-INH)
    - The different forms of HAE share some clinical features and, possibly, therapeutic options with HAE-1/2
    - Can only be diagnosed by genetic testing, which is becoming increasingly available
    - Genetic testing should be performed and include testing for the 6 recognized HAE types:
        - HAE with mutation in the factor XII gene (HAE-FXII)
        - HAE with mutation in the angiopoietin-1 gene (HAE-ANGPT1)
        - HAE with mutation in the plasminogen gene (HAE-PLG)
        - HAE with mutation in the kininogen 1 gene (HAE-KNG1)
        - HAE with mutation in the myoferlin gene (HAE-MYOF)
        - HAE with mutation in the heparan sulfate 3-O- sulfotransferase 6 gene (HAE-HS3ST6).
    - Additional mutations are likely to be identified in the future and should be included in the genetic diagnostic workup for HAE.

Type of Angioedema	Laboratory Findings		
	C4 Level	Antigenic C1 INH Level	Functional C1 INH Level
HAE – Type I	↓	↓	↓
HAE – Type II	↓	↔ or ↑	↓

Key: ↓ - decreased, ↑ - increased, ↔ - normal

(6) References

- AHFS®. Available by subscription at http://www.lexi.com
- 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. 2020; S2213-2198(20)30878-3. doi:10.1016/j.jaip.2020.08.046
- DrugDex®. Available by subscription at http://www.micromedexsolutions.com/home/dispatch
- Ruconest (C1 esterase inhibitor, recombinant) [Prescribing information]. Bridgewater, NJ: Pharming Healthcare Inc.; 4/2020.
- 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. 2022; 77: 1961–1990.

- 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: https://doi.org/10.1016/j.jaci.2013.03.034

1. 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. 2022; 77: 1961–1990.

(7) Policy Update

Date of last review: 1Q2023
Date of next review: 1Q2024
Changes from previous policy version:

- No clinical change to policy following routine annual review.

BSC Drug Coverage Criteria to Determine Medical Necessity
Reviewed by P&T Committee