MEDICAL MUTUAL®

Drug Policy

Policy:	**201512**	**Initial Effective Date:** **04/30/2015** **Annual Review Date:** **03/20/2025** **Last Revised Date:** **03/20/2025**
Code(s):	**HCPCS J0596**	
SUBJECT:	**Ruconest (recombinant C1 esterase inhibitor for IV use)**	

☒Subject to Site of Care

Prior approval is required for some or all procedure codes listed in this Corporate Drug Policy.

Initial and renewal requests for the medication(s) listed in this policy are subject to site of care management. When billed under the medical benefit, administration of the medication will be restricted to a non-hospital facility-based location (i.e., home infusion provider, provider's office, free-standing ambulatory infusion center) unless the member meets the site of care exception criteria. To view the exception criteria and a list of medications subject to site of care management please click here.

OVERVIEW

Ruconest is a recombinant C1-INH purified from milk of transgenic rabbits. Ruconest is indicated for the treatment of acute HAE attacks in adult and adolescent patients. The effectiveness of Ruconest was not established in HAE patients with laryngeal attacks. Also, the safety and efficacy of Ruconest for prophylactic therapy have not been established.

Hereditary angioedema is a rare, debilitating, potentially life-threatening genetic disorder caused by a deficiency in C1-INH, a plasma protein involved in the regulation of the complement and intrinsic coagulation pathways. Hereditary angioedema is caused by mutations in the C1-INH gene located on chromosome 11q and inherited as an autosomal dominant trait. Two main types of hereditary angioedema exist: mutations causing Type I hereditary angioedema are associated with decreased production of C1-INH leading to decreased functional levels; Type II hereditary angioedema mutations are associated with a dysfunctional C1 inhibitor, but the inhibitor level is normal.

HAE is characterized by recurrent episodes of nonpruritic, nonpitting, subcutaneous or submucosal edema associated with pain syndrome, nausea, vomiting, diarrhea, and/or life-threatening airway swelling. Airway obstruction due to swelling is life-threatening if left untreated. There is a wide variation in the frequency and severity of attacks. Clinical experience suggests that minor trauma and/or stress, among other triggers, may precipitate attacks. Untreated attacks typically last over 48 to 96 hours. Short-term prophylaxis with a C1-INH - is recommended if more than minor manipulation (e.g., mild dental work) is needed, and prior to intubation or major procedures. The dose for short-term prophylaxis with C1-INH varies from 10 U/kg to 20 U/kg or 1,000 units, 1 to 6 hours before procedure. Long-term prophylaxis should be considered in all severely symptomatic patients, taking into consideration the severity of disease, frequency of attacks, patient's quality of life, availability of resources, and failure to achieve adequate control by on-demand therapy.

MEDICAL MUTUAL®

Drug Policy

POLICY STATEMENT

This policy involves the use of Ruconest. Prior authorization is recommended for pharmacy and medical benefit coverage of Ruconest. Approval is recommended for those who meet the conditions of coverage in the **Criteria, Dosing (medical benefit requests only), Initial/Extended Approval, Duration of Therapy**, and **Labs/Diagnostics** for the diagnosis provided. **Waste Management** applies for all covered conditions that are administered by a healthcare professional. **Conditions Not Recommended for Approval** are listed following the recommended authorization criteria and Waste Management section. Requests for uses not listed in this policy will be reviewed for evidence of efficacy and for medical necessity on a case-by-case basis.

Because of the specialized skills required for evaluation and diagnosis of patients treated with Ruconest as well as the monitoring required for AEs and long-term efficacy, initial approval requires Ruconest be prescribed by or in consultation with a physician who specializes in the condition being treated. All approvals for initial therapy are provided for the initial approval duration noted below; if reauthorization is allowed, a response to therapy is required for continuation of therapy unless otherwise noted below.

The site of care medical necessity criteria applies to initial therapy and reauthorizations under the medical benefit only.

> Submission of medical records (chart notes) related to the medical necessity criteria is REQUIRED on all requests for authorizations. Records will be reviewed at the time of submission. Please provide documentation related to diagnosis, step therapy, and clinical markers (i.e., genetic and mutational testing) supporting initiation when applicable. Please provide documentation via direct upload through the PA web portal or by fax.

Medical Necessity:

Coverage will be provided when the following criteria have been met:

The requested medication will not be used for Hereditary Angioedema (HAE) Prophylaxis. Ruconest has no efficacy or dosing data for HAE prophylaxis, so it is not approved for this indication; AND

The requested medication will not be used to treat Hereditary Angioedema (HAE) Patients with Laryngeal Attacks. Effectiveness of Ruconest was not established in HAE patients with laryngeal attacks AND;

1. Hereditary Angioedema (HAE) Type 1 and 2 Treatment of Acute Attacks, Initial Therapy

Criteria. *Patient must meet the following criteria*

A. The patient has HAE as confirmed by following criteria:

a. Patient has low levels of functional C1-INH protein (< 50% of normal) as defined by the laboratory reference values [documentation required]; OR

   b. Patient has lower than normal serum C4 levels (< 14 mg/dL), as defined by the laboratory reference values AND lower than normal C1-INH level (< 19.9 mg/dL) [documentation required]; AND

B. The medication is prescribed by or in consultation with an allergist, immunologist, hematologist or a physician that specializes in the treatment of HAE or related disorders; AND

C. Provider has determined that patient does not have a known or suspected allergy to rabbits and rabbit-derived products; AND

D. All other causes of acquired angioedema (e.g., medications, auto-immune diseases) have been excluded; AND

E. Patient has at least ONE of the following criteria:

   a. Patient must have history of self-limiting, non-inflammatory subcutaneous angioedema, without uticaria, which is recurrent and lasts >12 hours; OR

   b. Self-limiting, recurrent abdominal pain without a clear organic cause lasting >6 hours; AND

F. Patient must NOT have HAE with laryngeal attacks; AND

G. Ruconest is not used in combination with other approved treatments for acute HAE attacks (e.g. Berinert, Firazyr, or Kalbitor); AND

H. Site of care medical necessity is met*.

2. <u>Patient has been started on Ruconest</u>

Criteria. *Patient must meet the following criteria*

A. The patient has HAE as confirmed by following criteria:

   a. Patient has low levels of functional C1-INH protein (< 50% of normal) as defined by the laboratory reference values [documentation required]; OR

   b. Patient has lower than normal serum C4 levels (< 14 mg/dL or as defined by the laboratory reference values) AND lower than normal C1-INH level (< 19.9 mg/dL or as defined by the laboratory reference values) [documentation required]; AND

B. The medication is prescribed by or in consultation with an allergist, immunologist, hematologist or a physician that specializes in the treatment of HAE or related disorders; AND

C. Provider has determined that patient does not have a known or suspected allergy to rabbits and rabbit-derived products; AND

D. All other causes of acquired angioedema (e.g., medications, auto-immune diseases) have been excluded; AND

E. Patient has at least ONE of the following criteria:

   a. Patient must have history of self-limiting, non-inflammatory subcutaneous angioedema, without uticaria, which is recurrent and lasts >12 hours; OR

   b. Self-limiting, recurrent abdominal pain without a clear organic cause lasting >6 hours; AND

F. Patient must NOT have HAE with laryngeal attacks; AND

G. Ruconest is not used in combination with other approved treatments for acute HAE attacks (e.g. Berinert, Firazyr, or Kalbitor); AND

H. Patient has at least 1 annual assessment by an HAE specialist; AND

I. The patient has had a favorable clinical response to treatment with Ruconest (e.g. decrease in the duration of HAE attacks, quick onset of symptom relief, complete resolution of symptoms, decrease in HAE acute attack frequency or severity); AND

J. Site of care medical necessity is met*.

Dosing in HAE Treatment of Acute Attacks. *Dosing must meet the following:* Recommended dose for patients less than 84 kilograms is 50 Units per kg to be administered as a slow intravenous injection over approximately 5 minutes. Recommended dose for patients 84 kilograms or greater is 4200 Units per kg to be administered as a slow intravenous injection over approximately 5 minutes. No more than two doses should be administered within a 24-hour period with a maximum of 4200 Units for each dose

Initial Approval/ Extended Approval.
A) *Initial Approval:* 1 year
B) *Extended Approval:* 1 year

Waste Management for All Indications.
Solution Reconstituted, Intravenous [preservative free]:
Ruconest: 2100 units (1 ea) [contains rabbit protein]

Documentation Requirements:

The Company reserves the right to request additional documentation as part of its coverage determination process. The Company may deny reimbursement when it has determined that the drug provided or services performed were not medically necessary, investigational or experimental, not within the scope of benefits afforded to the member and/or a pattern of billing or other practice has been found to be either inappropriate or excessive. Additional documentation supporting medical necessity for the services provided must be made available upon request to the Company. Documentation requested may include patient records, test results and/or credentials of the provider ordering or performing a service. The Company also reserves the right to modify, revise, change, apply and interpret this policy at its sole discretion, and the exercise of this discretion shall be final and binding.

REFERENCES

1. Ruconest® [prescribing information]. Raleigh, NC: Salix Pharmaceuticals, Inc.; April 2020
2. Maurer, Marcus et al. “The international WAO/EAACI guideline for the management of hereditary angioedema-The 2021 revision and update.” Allergy vol. 77,7 (2022): 1961-1990. doi:10.1111/all.15214
3. Craig T, Pursun EA, Bork K, et al. WAO guideline for the management of hereditary angioedema. WAO Journal. 2012;5:182-199.
4. Craig TJ, Schneider LC, MacGinnitie AJ.Plasma-derived C1-INH for managing hereditary angioedema in pediatric patients: A systematic review. Pediatr Allergy Immunol. 2015 Sep;26(6):537-44.
5. Genetic test indications and interpretations in patients with hereditary angioedema. Weiler CR, van Dellen RG. Mayo Clin Proc. 2006 Jul;81(7):958-72
6. Agostoni, Angelo, et al. "Hereditary and acquired angioedema: problems and progress: proceedings of the third C1 esterase inhibitor deficiency workshop and beyond." Journal of Allergy and Clinical Immunology 114.3 (2004): S51-S131.

7. C1 Esterase Inhibitor Recombinant. In: DRUGDEX [online database]. Truven Health Analytics. Greenwood Village, CO. Last updated 17 November 2017. Accessed on 21 March 2019.

Prior approval is required for HCPCS Codes J0596 and J3490 and J3590 or J9999

†When *unclassified drugs* (J3490) or *unclassified biologics* (J3590) or *unclassified antineoplastics* (J9999) is determined to be Ruconest

Edits and Denials:

Prior approval: Prior approval is required for Ruconest **(HCPCS Codes J0596)**. Requests for prior approval will be authorized by a nurse reviewer if submitted documentation meets criteria outlined within the Corporate Medical Policy.

Requests for prior approval will be forwarded to a qualified physician reviewer if submitted documentation does not meet criteria outlined within Corporate Medical Policy.

TOPPS: Claims received with **HCPCS Code J0596**will pend with **Remark Code M4M** and will be adjudicated in accordance with the Corporate Medical Policy. Claims received with **HCPCS Code J3590** will pend with **Remark Code PRR** and will be adjudicated in accordance with the Corporate Medical Policy.

Liability: A participating provider will be required to write off charges denied as not medically necessary.

HCPCS Code(s):	
J0596	Injection, C1 esterase inhibitor (recombminant), Ruconest, 10 units