MEDICAL MUTUAL®

Drug Policy

Policy:	**201512**	**Initial Effective Date: 04/30/2015**
Code(s):	**HCPCS J0596**	**Annual Review Date: 03/15/2018**
SUBJECT:	**Ruconest® (recombinant C1 esterase inhibitor for IV use – Salix Pharmaceuticals)**	**Last Revised Date: 08/16/2018**

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

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.

POLICY STATEMENT

This policy involves the use of Ruconest. Prior authorization is recommended for pharmacy benefit coverage of Ruconest. Approval is recommended for those who meet the conditions of coverage in the **Criteria and Initial/Extended Approval** for the diagnosis provided. **Conditions Not Recommended for Approval** are listed following the recommended authorization criteria. 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.

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Because of the specialized skills required for evaluation and diagnosis of patients treated with Ruconest as well as the monitoring required for adverse events 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.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Ruconest is recommended in those who meet the following criteria:

1. **Hereditary Angioedema (HAE) Type 1 and 2 Treatment of Acute Attacks, Initial Therapy.** Approve Ruconest if the patient meets the following criteria (a, b, c, d, e, f, g and h):

   a) The patient has HAE as confirmed by following criteria (i or ii):
   i) Patient has low levels of functional C1-INH protein (< 67% of normal) as defined by the laboratory reference values [documentation required]; OR
   ii) 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 (i or ii)
   i) Patient must have history of self-limiting, non-inflammatory subcutaneous angioedema, without uticaria, which is recurrent and lasts >12 hours; OR
   ii) 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. **Patient has been started on Ruconest.** Approve for, an indication or condition addressed as an approval in the Recommended Authorization Criteria (FDA-Approved Indications), continuation of therapy if the patient meets the following criteria (a, b, c, d, e, f, g, h and i):

   a) The patient has HAE as confirmed by following criteria (i or ii):
   i) Patient has low levels of functional C1-INH protein (< 67% of normal) as defined by the laboratory reference values[documentation required]; OR
   ii) 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 (i or ii)

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

ii.) 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) Site of care medical necessity is met*.

Dosing in HAE Treatment of Acute Attacks: Recommended dose is 50 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:* 365 days (1 year)
B) *Extended Approval:* 365 days (1 year)

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

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Ruconest has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval).

1. **Hereditary Angioedema (HAE) Prophylaxis.** Ruconest has no efficacy or dosing data for HAE prophylaxis, so it is not approved for this indication.
2. **Hereditary Angioedema (HAE) Patients with Laryngeal Attacks.** Effectiveness of Ruconest was not established in HAE patients with laryngeal attacks.
3. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

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

- Ruconest® [prescribing information]. Raleigh, NC: Salix Pharmaceuticals, Inc.; September 19, 2016
- Craig T, Pursun EA, Bork K, et al. WAO guideline for the management of hereditary angioedema. WAO Journal. 2012;5:182-199.
- 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.
- Genetic test indications and interpretations in patients with hereditary angioedema. Weiler CR, van Dellen RG. Mayo Clin Proc. 2006 Jul;81(7):958-72
- 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.

FOR MEDICAL BENEFIT COVERAGE REQUESTS:

*MMO Site of Care Medical Necessity Criteria:

Medications in this policy will be administered in a place of service that identifies the location to be a non-hospital facility based location (i.e., home infusion provider, provider's office, free-standing ambulatory infusion center) unless *at least one* of the following are met[†]:

1. Age less than 21 years; or
2. Clinically unstable based upon documented medical history (e.g., patient is hemodynamically unstable); or
3. History of a severe adverse event from previous administration of the prescribed medication; or
4. Requested medication is being administered as follows:
   - part of a chemotherapy regimen (e.g., anti-neoplastic agent, colony stimulating factor, erythropoiesis-stimulating agent, anti-emetic) for treatment of cancer; or
   - administered with dialysis; or
5. Physical or cognitive impairment and caregiver is not available to assist with safe administration of prescribed medication in the home; or

6. Up to 1 dose of medication or re-initiation after at least 12 months; or
7. Experiencing adverse events that are not managed by premedication or resources available at a non-hospital facility based location.

†This criterion does not apply to Medicare or Medicare Advantage members.

Prior approval is required for HCPCS Code J0596

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