Policy Title:	Ruconest (recombinant C1 esterase inhibitor) (Intravenous)		
		Department:	PHA
Effective Date:	01/01/2020		
Review Date:	12/20/2019, 1/22/20, 5/06/2021, 2/10/2022, 3/16/2023, 12/14/2023, 01/04/2024, 6/25/2025, 11/10/2025		

Purpose: To support safe, effective, and appropriate use of Ruconest (recombinant C1 esterase inhibitor).

Scope: Medicaid, Commercial, Medicare

Policy Statement:

Ruconest (recombinant C1 esterase inhibitor) is covered under the Medical Benefit when used within the following guidelines. Use outside of these guidelines may result in non-payment unless approved under an exception process.

Procedure:

Coverage of Ruconest (recombinant C1 esterase inhibitor) will be reviewed prospectively via the prior authorization process based on criteria below.

Summary of Evidence:

Ruconest is a recombinant human C1 esterase inhibitor indicated for the treatment of acute attacks of HAE. Clinical trials evaluating the efficacy and safety of Ruconest have demonstrated its effectiveness in rapidly resolving acute HAE attacks and reducing the duration of symptoms. In clinical trials, Ruconest demonstrated superiority over placebo in reducing the time to onset of symptom relief and achieving symptom resolution in patients with acute HAE attacks. The trials showed that Ruconest provided rapid and sustained relief of symptoms, including swelling, pain, and discomfort associated with HAE attacks. Commonly reported adverse reactions include headache, nausea, and diarrhea, which are generally mild to moderate in severity.

Initial Criteria:

- Member is 13 years of age or older; AND
- Ruconest is being used for treatment of acute hereditary angioedema (HAE) attacks
- Medication is prescribed by, or in consultation with allergist/immunologist or a physician who specializes in the management of HAE; AND
- Member has 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
- Member has documented diagnosis of HAE type I or type II and meets one of the following:

- Member has C1 inhibitor deficiency or dysfunction as confirmed by laboratory testing; and meets one of the following criteria:
    - C1 inhibitor (C1-INH) antigenic level below the lower limit of normal as defined by the laboratory performing the test, or
    - Normal C1-INH antigenic level and a low C1-INH functional level (functional C1-INH less than 50% or C1-INH functional level below the lower limit of normal as defined by the laboratory performing the test); OR
- Member has normal C1 inhibitor as confirmed by laboratory testing and meets one of the following criteria:
    - Member has an F12, angiopoietin-1, plasminogen, or kininogen-1 (KNG1), heparan sulfate-glucosamine 3-O-sulfotransferase 6 (HS3ST6), or myoferlin (MYOF) pathogenic variant as confirmed by genetic testing or
    - Member has a documented family history of angioedema, and the member's angioedema was refractory to a trial of high-dose antihistamine therapy (e.g., cetirizine 40 mg per day or the equivalent) for at least one month; AND

- The requested medication will not be used in combination with other products indicated for acute treatment of HAE attacks (e.g., Ekterly (sebetralstat), Berinert (C1 esterase inhibitor), , Kalbitor (ecallantide), or Icatibant),); AND
- Other causes of angioedema have been ruled out (e.g., angiotensin-converting enzyme inhibitor [ACE-I] induced an angioedema, angioedema related to an estrogen containing drug, allergic angioedema).
- For members 18 years of age and older, they have documentation that the member has had an inadequate response, intolerance, or contraindication to icatibant
- Medicare members who have previously received this medication within the past 365 days are not subject to Step Therapy Requirements.

Continuation of Therapy Criteria:

- Member continues to meet initial criteria; AND
- Documentation that the member has experienced reduction in severity and duration of attacks since starting treatment; AND
- Prophylaxis treatment should be considered based on the attack frequency, attack severity, comorbid conditions, and member's quality of life

Coverage durations:

- Initial coverage: 6 months
- Continuation of therapy coverage: 6 months

Per §§ 42 CFR 422.101, this clinical medical policy only applies to Medicare in the absence of National Coverage Determination (NCD) or Local Coverage Determination (LCD).

Policy Rationale:
Ruconest was reviewed by the Neighborhood Health Plan of Rhode Island Pharmacy & Therapeutics (P&T) Committee. Neighborhood adopted the following clinical coverage criteria to ensure that its members use Ruconest according to Food and Drug Administration (FDA) approved labeling and/or relevant clinical literature. Neighborhood worked with network prescribers and pharmacists to draft these criteria. These criteria will help ensure its members are using this drug for a medically accepted indication, while minimizing the risk for adverse effects and ensuring more cost-effective options are used first, if applicable and appropriate. For Medicare members, these coverage criteria will only apply in the absence of National Coverage Determination (NCD) or Local Coverage Determination (LCD) criteria. Neighborhood will give individual consideration to each request it reviews based on the information submitted by the prescriber and other information available to the plan.

Dosage/Administration:

Indication	Dose	Maximum dose (1 billable unit = 10 units)
HAE	Body weight < 84 kg: 50 international units (IU) per kg body weight by intravenous injection Body weight ≥ 84 kg: 4200 IU (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 IU per dose. No more than two doses should be administered within a 24-hour period.	3360 billable units per 28 days

Investigational use: All therapies are considered investigational when used at a dose or for a condition other than those that are recognized as medically accepted indications as defined in any one of the following standard reference compendia: American Hospital Formulary Service Drug information (AHFS-DI), Thomson Micromedex DrugDex, Clinical Pharmacology, Wolters Kluwer Lexi-Drugs, or Peer-reviewed published medical literature indicating that sufficient evidence exists to support use. Neighborhood does not provide coverage for drugs when used for investigational purposes.

Applicable Codes:
Below is a list of billing codes applicable for covered treatment options. The below tables are provided for reference purposes and may not be all-inclusive. Requests received with codes from tables below do not guarantee coverage. Requests must meet all criteria provided in the procedure section.

The following HCPCS/CPT codes are:

HCPCS/CPT Code	Description
J0596	Injection, c1 esterase inhibitor (recombinant), Ruconest, 10 units

References:

1. Ruconest [package insert]. Raleigh, NC: Santarus, Inc.; April 2020. Accessed October 2025.
2. 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.
3. Cicardi M, Bork K, Caballero T, et al. Hereditary Angioedema International Working Group. Evidence-based recommendations for the therapeutic management of angioedema owing to hereditary C1 inhibitor deficiency: consensus report of an International Working Group. *Allergy*. 2012;67:147-157.
4. 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: In Practice*. 2013; 1(5): 458-467.
5. 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(6):S145-S156.
6. Maurer M, Magerl M, Ansotegui I, et al. The international WAO/EAACI guideline for the management of hereditary angioedema – the 2017 revision and update. *Allergy*. 2018;00:1-22.