

Medical Policy:

Ruconest® (C1esterase inhibitor [recombinant])

POLICY NUMBER	LAST REVIEW	ORIGIN DATE
MG.MM.PH.36	March 28, 2025	July 25, 2018

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The treating physician or primary care provider must submit to EmblemHealth, or ConnectiCare, as applicable (hereinafter jointly referred to as “EmblemHealth”), the clinical evidence that the member meets the criteria for the treatment or surgical procedure. Without this documentation and information, EmblemHealth will not be able to properly review the request preauthorization or post-payment review. The clinical review criteria expressed below reflects how EmblemHealth determines whether certain services or supplies are medically necessary. This clinical policy is not intended to pre-empt the judgment of the reviewing medical director or dictate to health care providers how to practice medicine. Health care providers are expected to exercise their medical judgment in rendering appropriate care. Health care providers are expected to exercise their medical judgment in rendering appropriate care.

EmblemHealth established the clinical review criteria based upon a review of currently available clinical information (including clinical outcome studies in the peer reviewed published medical literature, regulatory status of the technology, evidence-based guidelines of public health and health research agencies, evidence-based guidelines and positions of leading national health professional organizations, views of physicians practicing in relevant clinical areas, and other relevant factors). EmblemHealth expressly reserves the right to revise these conclusions as clinical information changes and welcomes further relevant information. Each benefit program defines which services are covered. The conclusion that a particular service or supply is medically necessary does not constitute a representation or warranty that this service or supply is covered and/or paid for by EmblemHealth, as some programs exclude coverage for services or supplies that EmblemHealth considers medically necessary.

If there is a discrepancy between this guideline and a member's benefits program, the benefits program will govern. Identification of selected brand names of devices, tests and procedures in a medical coverage policy is for reference only and is not an endorsement of any one device, test or procedure over another. In addition, coverage may be mandated by applicable legal requirements of a state, the Federal Government or the Centers for Medicare & Medicaid Services (CMS) for Medicare and Medicaid members. All coding and web site links are accurate at time of publication.

EmblemHealth may also use tools developed by third parties, such as the MCG™ Care Guidelines, to assist us in administering health benefits. The MCG™ Care Guidelines are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice. EmblemHealth Services Company, LLC, has adopted this policy in providing management, administrative and other services to EmblemHealth Plan, Inc., EmblemHealth Insurance Company, EmblemHealth Services Company, LLC, and Health Insurance Plan of Greater New York (HIP) related to health benefit plans offered by these entities. ConnectiCare, an EmblemHealth company, has also adopted this policy. All of the aforementioned entities are affiliated companies under common control of EmblemHealth Inc.

Definitions

Hereditary angioedema is an autosomal dominant condition marked by unpredictable and recurrent potentially fatal angioedema attacks; treatment options include injectable drugs for prophylaxis or for acute attacks.

Length of Authorization

Approval will be granted for 6 months and may be renewed

Dosing Limits [Medical Benefit]

Max units (per dose and over time):

- 420 billable units per dose up to 2 times in a 24 hour period once per week
- 3360 billable units per 28 days

Guideline

I. INITIAL CRITERIA

1. Ruconest (C1 esterase inhibitor [recombinant]) is considered medically necessary for the treatment of acute attacks of **hereditary angioedema** and when the following criteria:
 - A. Patient is 13 years of age or older; **AND**
 - B. Ruconest is prescribed by, or in consultation with, a specialist in: allergy, immunology, hematology, pulmonology, or medical genetics; **AND**
 - C. Confirmation the member is avoiding medications known to cause angioedema (e.g., ACE inhibitors, oral contraceptives, hormone replacement therapy, Dipeptidyl peptidase IV (DPP-IV) inhibitors (e.g., sitagliptin), Neprilysin inhibitors (e.g., sacubitril); **AND**
 - D. Member has a history of moderate to severe cutaneous or abdominal attacks **OR** mild to severe airway swelling attacks of HAE (i.e. debilitating cutaneous/gastrointestinal symptoms laryngeal/pharyngeal/tongue swelling); **AND**
 - E. Member has one of the following clinical presentations (table below) consistent with HAE subtype:

HAE I (C1-inhibitor deficiency)
<ul style="list-style-type: none"> ▪ 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 <ul style="list-style-type: none"> ○ Member has a family history of HAE; OR ○ Normal C1q level
HAE II (C1-inhibitor dysfunction)
<ul style="list-style-type: none"> ▪ 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)
HAE with normal C1NH (formerly known as HAE III)
<ul style="list-style-type: none"> ▪ Normal C1-INH antigenic level; AND ▪ Normal C4 level; AND ▪ Normal C1-INH functional level; AND <ul style="list-style-type: none"> ○ Member has a known HAE-causing mutation (e.g., mutation of coagulation factor XII gene [F12 mutation], mutation in the angiotensin-converting enzyme 1 gene, mutation in the plasminogen gene); OR ○ Member has a family history of HAE

II. RENEWAL CRITERIA

Coverage for Ruconest (C1 esterase inhibitor [recombinant]) may be renewed when all of the following criteria are met:

1. Member continues to meet the criteria in the initial guideline; **AND**
2. Significant improvement in severity and duration of attacks have been achieved and sustained; **AND**
3. Absence of unacceptable toxicity from the drug (e.g., hypersensitivity reactions, thrombotic events, laryngeal attacks)

Limitations/Exclusions

1. Ruconest® (C1 esterase inhibitor [recombinant]) is contraindicated in patients with a history of allergy to rabbits or rabbit-derived products.
2. The cumulative amount of medication(s) the member 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 member 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

- Ruconest (C1 esterase inhibitor [recombinant]) is considered experimental or investigational for all other uses

Applicable Procedure Codes

Code	Description
J0596	Injection, C-1 esterase inhibitor (recombinant), Ruconest, 10units

Applicable NDCs

Code	Description
71274-0350-02	Ruconest 2100 units
71274-0350-01	Ruconest 2100 units
68012-0350-xx	Ruconest 2100 IU single use vial 25 mL vial

ICD-10 Diagnoses

Code	Description
D84.1	Defects in the complement system

Revision History

Company(ies)	DATE	REVISION
EmblemHealth & ConnectiCare	03/28/2025	Annual Review: No criteria changes
EmblemHealth & ConnectiCare	1/9/2024	Annual Review: No Criteria Changes, formatting changes, additional examples of medications to avoid added
EmblemHealth & ConnectiCare	5/09/2023	Annual Review: Added NDC 68012-0350-xx
EmblemHealth & ConnectiCare	1/11/2023	Transferred to New Template, added NDC codes
EmblemHealth & ConnectiCare	04/16/2020	Added to Limitations per FDA Label: Ruconest® (C1 esterase inhibitor [recombinant]) is contraindicated in patients with a history of allergy to rabbits or rabbit-derived products.
EmblemHealth & ConnectiCare	7/25/2018	Increased coverage duration to 6 months, removed confirmation patient is negative for helicobacter pylori infection, updated table describing clinical presentations consistent with HAE

References

1. Caballero T, Farkas H, Bouillet L, et al.; C-1-INH Deficiency Working Group. International consensus and practical guidelines on the gynecologic and obstetric management of female patients with hereditary angioedema caused by C1 inhibitor deficiency. *J Allergy Clin Immunol*. 2012; 129(2):308-320.
2. Cicardi M, Bork K, Caballero T, et al.; HAWK (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(2):147-157.
3. Craig T, Aygören-Pürsün EA, Bork K, et al. World Allergy Organization (WAO) guideline for the management of hereditary angioedema. *World Allergy Organ J*. 2012; 5(12):182-199.
4. Lang DM, Aberer W, Bernstein JA, et al. International consensus on hereditary and acquired angioedema. *Ann Allergy Asthma Immunol*. 2012; 109(6):395-402.
5. U.S. Hereditary Angioedema Association (HAEA) Advisory Board. HAEA Consensus Document: An approach to diagnosis and treatment of HAE. 2013. Available at: http://www.haea.org/wp-content/uploads/recommendations_2013.pdf. Accessed on October June 6, 2017.
6. Zuraw BL, Banerji A, Bernstein J, et al. U.S. Hereditary Angioedema Association (US HAE) Medical Advisory Board 2013 recommendations for the management of hereditary angioedema due to C1 inhibitor deficiency. *J Allergy Clin Immunol*. 2013a; 1(5):458-467.
7. Specialty-matched clinical peer review.