BlueCross BlueShield
Federal Employee Program
Blue Cross Blue Shield Association
750 9th St NW, Suite 900
Washington, D.C. 20001
1-800-624-5060
Fax 1-877-378-4727

5.85.017

Section:	Prescription Drugs	**Effective Date:**	October 1, 2025
Subsection:	Hematological Agents	**Original Policy Date:**	August 22, 2014
Subject:	Ruconest	**Page:**	1 of 5

Last Review Date: September 19, 2025

Ruconest

Description

Ruconest (C1 esterase inhibitor [recombinant])

Background
Ruconest is a human recombinant C1-esterase inhibitor for the treatment of acute attacks in adult and adolescent patients with hereditary angioedema (HAE). Hereditary angioedema is caused by having insufficient amounts of a plasma protein called C1-esterase inhibitor. People with HAE can develop rapid swelling of various parts of the body. Swelling of the airway is potentially fatal without immediate treatment. Ruconest is intended to restore the level of functional C1-esterase inhibitor in a patient's plasma, thereby treating the acute attack of swelling (1).

Regulatory Status
FDA-approved indication: Ruconest is a C1 esterase inhibitor [recombinant] indicated for the treatment of acute attacks in adult and adolescent patients with hereditary angioedema (HAE) (1).

Limitations of Use:
Effectiveness was not established in HAE patients with laryngeal attacks (1).

Patients, with known risk factors, should be monitored for thromboembolic (TE) events during and after Ruconest administration. Serious arterial and venous thromboembolic (TE) events have been reported at the recommended dose of plasma derived C1 esterase inhibitor products in patients with risk factors. Risk factors may include the presence of an indwelling venous

catheter/access device, prior history of thrombosis, underlying atherosclerosis, use of oral contraceptives or certain androgens, morbid obesity, and immobility (1).

The safety and efficacy of Ruconest in pediatric patients less than 13 years of age have not been established (1).

Related policies
Berinert, Cinryze, Haegarda, Icatibant, Kalbitor, Orladeyo, Takhzyro

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Ruconest may be considered **medically necessary** if the conditions indicated below are met.

Ruconest may be considered **investigational** for all other indications.

Prior-Approval Requirements

Age 13 years of age and older

Diagnosis

Patient must have the following:

1. Hereditary Angioedema (HAE) with **ONE** of the following:
    a. Patient has a C1 inhibitor deficiency or dysfunction as confirmed by laboratory testing **AND ALL** of the following:
        i. C4 level below the lower limit of normal as defined by the laboratory performing the test
        ii. 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)
    b. Patient has normal C1 inhibitor as confirmed by laboratory testing **AND ONE** of the following:
        i. F12, angiopoietin-1, plasminogen, or kininogen-1 (KNG1) gene

mutation as confirmed by genetic testing

ii. Documented family history of angioedema and the angioedema was refractory to a trial of high-dose antihistamine (e.g., cetirizine) for at least one month

AND ALL of the following:

a. Used for acute attacks of hereditary angioedema
b. **NOT** being used for the routine prevention of hereditary angioedema attacks
c. **NOT** being used to treat laryngeal attacks
d. **NO** dual therapy with another agent for treating acute attacks of hereditary angioedema (e.g., Berinert, Firazyr/Sajazir, Kalbitor)

Prior – Approval *Renewal* Requirements

Age 13 years of age and older

Diagnosis

Patient must have the following:

Hereditary Angioedema (HAE)

AND ALL of the following:

a. Used for acute attacks of hereditary angioedema
b. **NOT** being used for the routine prevention of hereditary angioedema attacks
c. **NOT** being used to treat laryngeal attacks
d. Patient has experienced a reduction in severity and/or duration of hereditary angioedema attacks
e. **NO** dual therapy with another agent for treating acute attacks of hereditary angioedema (e.g., Berinert, Firazyr/Sajazir, Kalbitor)

Policy Guidelines

Pre - PA Allowance

None

Prior - Approval Limits

Duration 12 months

Prior – Approval *Renewal* Limits

Same as above

Rationale

Summary

Ruconest is a C1-esterase inhibitor [recombinant] indicated for the treatment of acute attacks in adult and adolescent patients with hereditary angioedema (HAE). Effectiveness was not established in HAE patients with laryngeal attacks. Serious arterial and venous thromboembolic (TE) events have been reported at the recommended dose of plasma derived C1 esterase inhibitor products in patients with risk factors. The safety and efficacy of Ruconest in pediatric patients less than 13 years of age have not been established (1).

Prior authorization is required to ensure the safe, clinically appropriate, and cost-effective use of Ruconest while maintaining optimal therapeutic outcomes.

References

1. Ruconest [package insert]. Bridgewater, NJ: Pharming Healthcare Inc.; April 2020.

Policy History

Date	Action
August 2014	Addition to PA
December 2014	Annual editorial review and reference update
December 2015	Annual editorial review
December 2016	Annual editorial review and reference update Policy code changed from 5.10.17 to 5.85.17
September 2017	Annual review and reference update
December 2017	Annual review
September 2018	Annual review and reference update
November 2018	Annual review
September 2019	Annual review
September 2020	Annual review and reference update
March 2021	Annual editorial review and reference update
April 2021	Added initiation requirements including C1 inhibitor testing, C4 testing, C1-INH testing, gene mutation testing, or documented family history of refractory angioedema and continuation requirement for significant

	reduction in severity and/or duration of HAE attacks since starting therapy per FEP
June 2021	Annual review
October 2021	Added Sajazir to no dual therapy list
December 2021	Annual review
September 2022	Annual review
September 2023	Annual review
December 2023	Annual review
September 2024	Annual review
December 2024	Annual review
September 2025	Annual review

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on September 19, 2025 and is effective on October 1, 2025.