

5.85.05

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Subsection:	Hematological Agents	Original Policy Date:	December 7, 2011
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Last Review Date: March 12, 2021

Cinryze

Description

Cinryze (C1 esterase inhibitor [human])

Background

Cinryze is a C1-esterase inhibitor used for the treatment routine prophylaxis against angioedema attacks 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 the hands, feet, limbs, face, intestinal tract, or airway. These acute attacks of swelling can occur spontaneously, or can be triggered by stress, surgery or infection. Swelling of the airway is potentially fatal without immediate treatment. Cinryze is intended to restore the level of functional C1-esterase inhibitor in a patient's plasma, thereby preventing the acute attack of swelling (1-4).

Regulatory Status

FDA-approved indication: Cinryze is a C1 esterase inhibitor indicated for routine prophylaxis against angioedema attacks in adults, adolescents and pediatric patients (6 years of age and older) with Hereditary Angioedema (HAE) (2).

Hypersensitivity reactions may occur. Epinephrine should be immediately available to treat any acute severe hypersensitivity reactions following discontinuation of administration (2).

Thrombotic events have been reported at the recommended dose of C1 Esterase Inhibitor (human) products, including Cinryze, following treatment of HAE. Monitor closely patients with known risk factors for thrombotic events (2).

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Cinryze is made from human plasma and may contain infectious agents, e.g., viruses and, theoretically, the Creutzfeldt-Jakob disease (CJD) agent (2).

Related policies

Berinert, Firazyr, Haegarda, Kalbitor, Orladeyo, Ruconest, 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.

Cinryze may be considered **medically necessary** in patients 6 years of age or older for the routine prevention of hereditary angioedema (HAE) attacks and if the conditions indicated below are met.

Cinryze may be considered **investigational** in patients less than 6 years of age and for all other indications. .

Prior-Approval Requirements

Age 6 years of age and older

Diagnosis

Patient must have **ALL** of the following:

1. Hereditary Angioedema (HAE)
 - a. Routine prevention of angioedema attacks
 - b. **NO** dual therapy with other agents for the prevention of hereditary angioedema attacks
 - c. Inadequate treatment response or intolerance to a short-term course (5-days or less) of an androgen such as danazol, or a contraindication to one such as:
 - i. Undiagnosed abnormal genital bleeding
 - ii. Markedly impaired hepatic, renal, or cardiac function
 - iii. Pregnancy (member is currently pregnant or may become pregnant)
 - iv. Breast feeding
 - v. Porphyria
 - vi. Androgen-dependent tumor

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- vii. Active thrombosis or history of thromboembolic disease
- viii. Prepubertal child

Prior – Approval *Renewal* Requirements

Age 6 years of age and older

Diagnosis

Patient must have **ALL** of the following:

1. Hereditary Angioedema (HAE)
 - a. Routine prevention of angioedema attacks
 - b. **NO** dual therapy with other agents for the prevention of hereditary angioedema attacks

Policy Guidelines

Pre - PA Allowance

None

Prior - Approval Limits

Duration 12 months

Prior – Approval *Renewal* Limits

Same as above

Rationale

Summary

Cinryze is a C1 esterase inhibitor indicated for routine prophylaxis against angioedema attacks in adolescent and adult patients with Hereditary Angioedema (HAE). HAE symptoms include episodes of edema (swelling) in various body parts including the hands, feet, face, and airway. HAE is caused by mutations to C1-esterase-inhibitor (C1-INH). Serious arterial and venous thromboembolic (VTE) 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 Cinryze in

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children less than 6 years of age has not been established. Persons who experience frequent and/or severe episodes may be candidates for prophylactic treatment (1-4).

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

References

1. Zuraw BL. Clinical practice. Hereditary angioedema. N Engl J Med. Sep 4 2008;359(10):1027-36.2.
2. Cinryze [package insert]. Lexington, MA: ViroPharma Biologics, Inc.; January 2021.
3. 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.
4. Wintenberger C, Boccon-Gibod I, Launay D, et al. Tranexamic acid as maintenance treatment for non-histaminergic angioedema: analysis of efficacy and safety in 37 patients. Clin Exp Immunol 2014; 178:112.

Policy History

Date	Action
December 2011	New Policy
September 2012	Annual Review with editorial and reference update
March 2013	Annual editorial review and reference update
March 2014	Annual review and reference update
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 5.10.05 to 5.85.05
September 2017	Annual review and reference update
December 2017	Annual editorial review and reference update Addition of no dual therapy with other C1-esterase inhibitors for the prevention of angioedema attacks Addition of inadequate treatment response, intolerance, or contraindication to a danazol or tranexamic acid per SME
March 2018	Annual review
July 2018	Change in age from 12 years of age and older to 6 years of age and older
August 2018	Changed wording of no dual therapy requirement
September 2018	Annual review

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November 2018	Annual review. Removal of requirement to try and fail tranexamic acid and reworded danazol or androgen trial requirement per SME
September 2019	Annual review
September 2020	Annual review
March 2021	Annual editorial review and reference update

[Keywords](#)

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on March 12, 2021 and is effective on April 1, 2021.