

Specialty Guideline Management

Cinryze

Products Referenced by this Document

Drugs that are listed in the following table include both brand and generic and all dosage forms and strengths unless otherwise stated. Over-the-counter (OTC) products are not included unless otherwise stated.

Brand Name	Generic Name
Cinryze	C1 esterase inhibitor [human]

Indications

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-approved Indications¹

Cinryze is indicated for routine prophylaxis against angioedema attacks in adults, adolescents and pediatric patients (6 years of age and older) with hereditary angioedema (HAE).

All other indications are considered experimental/investigational and not medically necessary.

Documentation

Submission of the following information is necessary to initiate the prior authorization review:

- For initial authorization, the following should be documented:
 - C1 inhibitor functional and antigenic protein levels
 - F12, angiopoietin-1, plasminogen, kininogen-1 (KNG1), heparan sulfate-glucosamine 3-O-sulfotransferase 6 (HS3ST6), or myoferlin (MYOF) gene mutation testing, if applicable

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- Chart notes confirming family history of angioedema and the angioedema was refractory to a trial of high-dose antihistamine therapy, if applicable
- For continuation of therapy, chart notes demonstrating a reduction in frequency of attacks.

Prescriber Specialties

This medication must be prescribed by or in consultation with a prescriber who specializes in the management of HAE.

Coverage Criteria

Hereditary angioedema (HAE)¹⁻¹⁷

Authorization of 12 months may be granted for prevention of hereditary angioedema attacks when the requested medication will not be used in combination with any other medication used for the prophylaxis of HAE attacks and both of the following criteria are met at the time of diagnosis:

- Member meets either of the following criteria:
 - 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).
 - Member has normal C1 inhibitor as confirmed by laboratory testing and meets one of the following criteria:
 - Member has an F12, angiopoietin-1, plasminogen, kininogen-1 (KNG1), heparan sulfate-glucosamine 3-O-sulfotransferase 6 (HS3ST6), or myoferlin (MYOF) gene mutation as confirmed by genetic testing, or
 - Member has a documented family history of angioedema and the angioedema was refractory to a trial of high-dose antihistamine therapy (i.e., cetirizine at 40 mg per day or the equivalent) for at least one month.
- Other causes of angioedema have been ruled out (e.g., angiotensin-converting enzyme inhibitor [ACE-I] induced angioedema, angioedema related to an estrogen-containing drug, allergic angioedema).

Continuation of Therapy

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Authorization of 12 months may be granted for continuation of therapy when all of the following criteria are met:

- Member meets all requirements in the coverage criteria section.
- Member has experienced a significant reduction in frequency of attacks (e.g., $\geq 50\%$) since starting treatment.
- Member has reduced the use of medications to treat acute attacks since starting treatment.

References

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4. 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.
5. Busse PJ, Christiansen, SC, Riedl MA, et al. US HAEA Medical Advisory Board 2020 Guidelines for the Management of Hereditary Angioedema. *J Allergy Clin Immunol: In Practice*. 2021 Jan;9(1):132-150.e3.
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14. Bernstein, J. Severity of Hereditary Angioedema, Prevalence, and Diagnostic Considerations. *Am J Med*. 2018;24:292-298.

Reference number(s)
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17. Veronez CL, Csuka D, Sheik FR, et al. The expanding spectrum of mutations in hereditary angioedema. *J Allergy Clin Immunol Pract.* 2021;S2213-2198(21)00312-3.