

SPECIALTY GUIDELINE MANAGEMENT

CINRYZE (C1 esterase inhibitor [human])

POLICY

I. 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 Indication

Routine prophylaxis against angioedema attacks in adults, adolescents and pediatric patients (6 years of age or older) with hereditary angioedema (HAE)

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

II. DOCUMENTATION

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

- A. For initial authorization, the following should be documented:
 - 1. C4 levels and C1 inhibitor functional and antigenic protein levels
 - 2. F12, angiopoietin-1, plasminogen, or kininogen-1 (KNG1) gene mutation testing, if applicable
 - 3. Chart notes confirming family history of angioedema, if applicable
- B. For continuation of therapy, chart notes demonstrating a reduction in frequency of attacks

III. CRITERIA FOR INITIAL APPROVAL

Hereditary angioedema (HAE)

Authorization of 6 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 either of the following criteria is met:

- A. Member has C1 inhibitor deficiency or dysfunction as confirmed by laboratory testing and meets both of the following criteria:
 - 1. Member has a C4 level below the lower limit of normal as defined by the laboratory performing the test, and
 - 2. Member meets one of the following criteria:
 - i. C1 inhibitor (C1-INH) antigenic level below the lower limit of normal as defined by the laboratory performing the test, or
 - ii. 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. Member has normal C1 inhibitor as confirmed by laboratory testing and meets one of the following criteria:
 - 1. Member has an F12, angiopoietin-1, plasminogen, or kininogen-1 (KNG1) gene mutation as confirmed by genetic testing, or
 - 2. Member has a 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.

IV. CONTINUATION OF THERAPY

Authorization of 6 months may be granted for continuation of therapy when all of the following criteria are met:

- A. Member meets the criteria for initial approval.
- B. Member has experienced a significant reduction in frequency of attacks (e.g. $\geq 50\%$) since starting treatment.
- C. Member has reduced the use of medications to treat acute attacks.

V. REFERENCES

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3. Cicardi M, Bork K, Caballero T, et al. 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. 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. 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.
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7. Lang DM, Aberer W, Bernstein JA, et al. International consensus on hereditary and acquired angioedema. *Ann Allergy Asthma Immunol*. 2012; 109:395-402.
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13. Farkas H, Martinez-Saguer I, Bork K, et al. International consensus on the diagnosis and management of pediatric patients with hereditary angioedema with C1 inhibitor deficiency. *Allergy*. 2017;72(2):300-313.
14. Henao MP, Kraschewski J, Kelbel T, Craig T. Diagnosis and screening of patients with hereditary angioedema in primary care. *Therapeutics and Clin Risk Management*. 2016; 12: 701-711.
15. Bernstein, J. Severity of Hereditary Angioedema, Prevalence, and Diagnostic Considerations. *Am J Med*. 2018;24:292-298.