

## Medical Policy Manual **Approved Rev: Do Not Implement until 3/4/25**

### C1 Esterase Inhibitor (Human) Cinryze®

#### IMPORTANT REMINDER

We develop Medical Policies to provide guidance to Members and Providers. This Medical Policy relates only to the services or supplies described in it. The existence of a Medical Policy is not an authorization, certification, explanation of benefits or a contract for the service (or supply) that is referenced in the Medical Policy. For a determination of the benefits that a Member is entitled to receive under his or her health plan, the Member's health plan must be reviewed. If there is a conflict between the medical policy and a health plan or government program (e.g., TennCare), the express terms of the health plan or government program will govern.

#### 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

Cinryze is indicated for 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. C1 inhibitor functional and antigenic protein levels
  2. F12, angiotensin-1, plasminogen, kininogen-1 (KNG1), heparan sulfate-glucosamine 3-O-sulfotransferase 6 (HS3ST6), or myoferlin (MYOF) gene mutation testing, if applicable
  3. Chart notes confirming family history of angioedema and the angioedema was refractory to a trial of high-dose antihistamine therapy, if applicable
- B. For continuation of therapy, chart notes demonstrating a reduction in frequency of attacks

##### III. PRESCRIBER SPECIALTIES

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

##### IV. 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 **both** of the following criteria **are** met at the time of diagnosis:

##### **A. Member meets either of the following criteria:**

1. Member has C1 inhibitor deficiency or dysfunction as confirmed by laboratory testing and meets one of the following criteria:



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- 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).
  2. Member has normal C1 inhibitor as confirmed by laboratory testing and meets one of the following criteria:
    - i. Member has an F12, angiotensin-1, plasminogen, kininogen-1 (KNG1), heparan sulfate-glucosamine 3-O-sulfotransferase 6 (HS3ST6), or myoferlin (MYOF) gene mutation as confirmed by genetic testing, or
    - ii. 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.
- B. 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).**

### V. 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 since starting treatment.

### APPLICABLE TENNESSEE STATE MANDATE REQUIREMENTS

BlueCross BlueShield of Tennessee's Medical Policy complies with Tennessee Code Annotated Section 56-7-2352 regarding coverage of off-label indications of Food and Drug Administration (FDA) approved drugs when the off-label use is recognized in one of the statutorily recognized standard reference compendia or in the published peer-reviewed medical literature.

### ADDITIONAL INFORMATION

For appropriate chemotherapy regimens, dosage information, contraindications, precautions, warnings, and monitoring information, please refer to one of the standard reference compendia (e.g., the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) published by the National Comprehensive Cancer Network®, Drugdex Evaluations of Micromedex Solutions at Truven Health, or The American Hospital Formulary Service Drug Information).

### REFERENCES

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**EFFECTIVE DATE** 3/4/2025

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