

## Medical Policy Manual

### C1 Esterase Inhibitor

#### DESCRIPTION

C1 esterase inhibitor (C1-INH) is a normal constituent of human blood and is a serine proteinase inhibitor or serpin. C1-INH's primary function is to regulate the activation of the complement and intrinsic coagulation pathway. It also has a role in regulation of the fibrinolytic system. Commercially, C1-INH is derived from purified human plasma which has undergone multiple viral reduction steps.

Individuals with an inherited deficiency of C1-INH suffer from sudden, recurrent edematous swellings of the subcutaneous or submucosal tissues. This condition is known as hereditary angioedema (HAE).

An example of a preparation of C1-INH to prevent HAE attacks is Cinryze®.

An example of a preparation of C1-INH to treat abdominal or facial attacks of HAE is Berinert®.

#### REFER TO DECISION SUPPORT TREE

#### POLICY

- C1 esterase inhibitor (C1-INH) for the prevention of angioedema attacks is considered **medically necessary** if the medical appropriateness criteria are met. (See **Medical Appropriateness** below.)
- C1 esterase inhibitor (C1-INH) for the treatment of angioedema attacks is considered **medically necessary** if the medical appropriateness criteria are met. (See **Medical Appropriateness** below.)
- C1-INH for the treatment of other conditions/diseases is considered **investigational**.

#### MEDICAL APPROPRIATENESS

- C1 esterase inhibitor (C1-INH) for the prevention of angioedema attacks is considered **medically appropriate** if **ALL** of the following criteria are met:
  - The individual has a diagnosis of hereditary angioedema (HAE). (**Note:** Hereditary angioedema requires laboratory testing to confirm the diagnosis: C4 levels are decreased in virtually all individuals during an attack. Functional C1-INH levels are generally decreased in those with this diagnosis.)
  - The agent requested is Cinryze®.
- C1 esterase inhibitor (C1-INH) for the treatment of angioedema attacks is considered **medically appropriate** if **ALL** of the following criteria are met:
  - The individual has a diagnosis of hereditary angioedema (HAE). (**Note:** Hereditary angioedema requires laboratory testing to confirm the diagnosis: C4 levels are decreased in virtually all individuals during an attack. Functional C1-INH levels are generally decreased in those with this diagnosis.)
  - Attacks are acute
  - Location of the attacks is **ANY ONE** of the following
    - Abdomen
    - Face
  - The agent requested is Berinert®.

#### APPLICABLE TENNESSEE STATE MANDATE REQUIREMENTS

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Tennessee State law requires coverage of off-label indications of Food and Drug Administration (FDA) approved drugs when the off-label use is relative to life-threatening illnesses, such as cancer, AIDS, and coronary heart disease and recognized in one of the standard reference compendia (As defined in the statute: The United States Pharmacopoeia Drug Information, The American Medical Association Drug Evaluations, & The American Hospital Formulary Service Drug Information) or in the medical literature. This law is applicable to all fully insured members. The law is not applicable to self-funded accounts, but coverage for off-label uses may be provided based on the contractual agreement. **See Benefit Summary Specialty Pharmacy Tab.**

### ADDITIONAL INFORMATION

For appropriate dosage information, contraindications, precautions, warnings, and monitoring information, please refer to one of the standard reference compendia (e.g., The American Hospital Formulary Service Drug Information).

Hereditary angioedema (HAE) occurs in two main types: type I, accounting for 85% of cases, with C1 inhibitor (C1-INH) mutations throughout the gene and type II with mutations on or near exon 8 (15% of cases). HAE requires laboratory testing to confirm the diagnosis. C4 level testing during an HAE attack is a cost effective screen for the condition as an individual's C4 level is decreased in virtually all true HAE attacks. The diagnosis of HAE is confirmed for most patients by testing for decreased levels of antigenic C1-INH and functional C1-INH, although levels of antigenic C1-INH are normal in individuals with type II HAE.

No controlled studies were found in the published literature that validate the use of either preparation of C1 esterase inhibitor for the prophylaxis, treatment or prevention of any other condition/disease.

### SOURCES

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## Pharmaceutical Decision Support Tree

### **C1 Esterase Inhibitor (Cinryze<sup>®</sup>), Berinert<sup>®</sup>)**

1. Does the individual have angioedema attacks marked by a decreased C4 level?

If yes, go to question # 2

If no, this does not meet medical necessity and/or medical appropriateness criteria

2. Does the individual have a diagnosis of hereditary angioedema (HAE) confirmed by decreased functional C1 inhibitor (C1-INH) level?

If yes, go to question # 3

If no, this does not meet medical necessity and/or medical appropriateness criteria

3. Is Cinryze<sup>®</sup> the agent requested with a dosage of 1000 units intravenous every 3 or 4 days per routine prophylaxis against HAE attacks as stated in the FDA approved labeling?

If yes, this meets medical necessity and/or medical appropriateness criteria

If no, go to question #4

4. Is Berinert<sup>®</sup> the agent requested for the treatment of angioedema attacks with all the following?

- Attacks are acute
- Location of the attacks is abdominal or facial

If yes, this meets medical necessity and/or medical appropriateness criteria

If no, this does not meet medical necessity and/or medical appropriateness criteria