

**Complete Patient and Physician information (PLEASE PRINT)**

STEP  
1

Member Name:	Physician Name:
Address:	Address:
Member ID:	Phone #:
Member DOB:	Fax #:
	Tax ID or NPI Number:

**If Applicable:** Pharmacy Name: \_\_\_\_\_  
 Pharmacy Phone: \_\_\_\_\_

**Complete the Clinical Assessment:**

STEP  
2

Diagnosis	<input type="checkbox"/> For prophylaxis against angioedema attacks in adults and adolescents with Hereditary Angioedema (HAE) <input type="checkbox"/> Other (please state): _____ _____ _____
Clinical Consideration	<b>Please indicate any of the following that apply:</b> <input type="checkbox"/> Patient has a history of at least 1 severe event per month  <input type="checkbox"/> Patient has tried and failed or is intolerant to at least one other prior therapy, including 17 alpha-alkylated androgens (e.g. danazol, stanozolol) or an anti-fibrinolytic agent (e.g. tranexamic acid) for HAE prophylaxis (documentation required).
Physician Specialty	Diagnosis made by: <input type="checkbox"/> Immunologist <input type="checkbox"/> Allergist <input type="checkbox"/> Other (please state):
Supporting Documentation	Diagnosis: ICD-9 Code #/ Description / J Code (required):
	Please attach a copy of the prescription or provide ALL of the information below: Cinryze <sup>®</sup> (C1 esterase inhibitor)  Strength _____ Sig _____ Qty _____ Refills _____
	<p style="text-align: center;"><i>*Please attach all relevant medical records and test results*</i></p> <p style="text-align: center;"><b>We will not process incomplete forms.</b></p> <p style="text-align: center;"><b>If we do not receive the completed form &amp; all relevant medical records &amp; test results within 10 calendar days of this request, it will be denied.</b></p>

STEP  
3

**I certify that the above is correct and accurate to the best of my knowledge and that the form is complete. (please sign and date)**

\_\_\_\_\_  
 Prescriber Signature

\_\_\_\_\_  
 Date

STEP  
4

**Fax completed form to the Rocky Mountain Health Plans Pharmacy Help Desk:  
 970-248-5034**

Name of Person filling out form: \_\_\_\_\_

Pharmacy Technician initials \_\_\_\_\_ Date Initiated \_\_\_\_\_

**Confidentiality Notice:**

This facsimile transmission (and/or documents accompanying it) may contain confidential information. This information is intended only for the use of the individual(s) named above. If you have received this transmission in error, or cannot identify the recipient for distribution purposes, please notify us immediately at 970-244-7760. Plans underwritten by Rocky Mountain HMO or Rocky Mountain HealthCare Options. 11/08/11

## RMHP Formulary Coverage Policy

THIS INFORMATION IS NOT ALL-INCLUSIVE AND IS PROVIDED FOR INFORMATIONAL PURPOSES ONLY

# C1 Esterase Inhibitor, Human (Cinryze® and Berinert®)

## CLASSIFICATION

- Immune modulators

## DESCRIPTION

- Hereditary Angioedema (HAE) is a rare, chronic disorder affecting around 1 in 50,000 people. It is marked by recurring, acute swelling attacks at various body sites. This may be life threatening in some cases. For example, laryngeal involvement can cause serious airway constriction. Upper airway attacks are thought to occur in one-half to two-thirds of patients. Symptoms usually begin to resolve spontaneously within 48-72 hours. Attacks are often, but not always, trigger mediated and it is very difficult to identify exact attack triggers. The average HAE patient experiences about 20 attacks per year.
- Three types of HAE are identified. Type I is characterized by low plasma levels of C1-inhibitor (C1-INH), and accounts for about 85% of cases. Type II is characterized by normal plasma C1-inhibitor, but not all is functional. Type III is more idiopathic, occurs predominantly in women, appears to be estrogen-dependant, and may result from certain gene mutations (factor XII)
- Lack of CI-INH means certain physiological reactions in the plasma go unchecked. Historically, the main concern in HAE was thought to be uncontrolled activation of the complement system, but more recent studies point towards excess bradykinin as the active substrate.
- HAE usually begins to manifest itself during childhood or infancy.
- Therapy for HAE has traditionally consisted of attenuated androgens, antifibrinolytic drugs, and use of fresh frozen plasma (FFP). Attenuated androgens are only for prophylaxis, antifibrinolytics help decrease the frequency and intensity of attacks (not as effectively as androgens), and FFP is used during acute attacks (though it can actually worsen attacks due to complement components in human plasma, as well as other safety concerns).
- C1-esterase inhibitors (C1-INH) have been available in Europe for many years and have become a first-line therapy in many countries. Cinryze® was the first C1-INH to gain FDA approval in October 2008.
- No US guidelines seem to address appropriate prophylaxis in HAE. However, Canadian and British guidelines suggest that prophylaxis is warranted when there is at least one serious event per month and that C1 esterase inhibitor therapy is recommended when patients have failed (or cannot tolerate) attenuated androgens or antifibrinolytics.
- Cinryze® is FDA approved for ***routine prophylaxis*** against angioedema attacks in adolescent and adult patients with Hereditary Angioedema (HAE). This was established by a 24-week, multi-center, randomized, double-blind, placebo-controlled, crossover, clinical trial (n=24) which demonstrated that prophylaxis with Cinryze® was superior to placebo in reduction of swelling episodes in adult and adolescent patients with hereditary

angioedema. In a smaller trial, Cinryze was noted to be effective in reducing the median number of angioedema attacks per year in 22 adult patients with severe hereditary angioedema who were intolerant to or not responding to danazol (an attenuated androgen). Adolescents (age 9 and above) were included in another placebo controlled trial where efficacy was established versus placebo.

- Berinert® is FDA approved for ***the treatment of acute abdominal or facial attacks*** of HAE in adult and adolescent patients greater than 12 years of age. In a double-blind, prospective, multinational, parallel-group, dose finding, three-arm, clinical study (n=124; 6 to 72 years of age) of Berinert for the treatment of acute abdominal or facial attacks of hereditary angioedema (HAE), patients treated with Berinert(R) 20 units/kilogram achieved a significant decrease in time to onset of relief of symptoms of HAE attack compared with placebo (median of 30 minutes for Berinert(R) versus 1.5 hours for placebo; p=0.0025). The safety and efficacy of Berinert for prophylactic therapy have not been established.
- Kalbitor® is FDA approved for ***the treatment of acute attacks*** of HAE. This agent inhibits plasma kallikrein, which is a factor produced unchecked in C1-INH deficiency. The safety and efficacy of ecallantide for the treatment of acute attacks of hereditary angioedema (HAE) was established in 2 randomized, double-blind, placebo-controlled trials (n=168). A significantly greater proportion of patients treated with ecallantide 40 milligrams/square meter for a hereditary angioedema attack achieved a successful outcome compared with placebo in this double-blind, placebo-controlled, ascending-dose study (n=48). Due to the risk of anaphylaxis, a REMS program was established to require administration by a physician who has support available to manage anaphylaxis.

## FORMULARY COVERAGE

Prior authorization:	Required
Good Health Formulary:	Tier 6
Commercial Formulary:	Tier 6
Medicare Part D coverage:	Tier 5

## COVERAGE CRITERIA

Cinryze® (C1 esterase inhibitor) meets the definition of **medical necessity** for the following:

- Routine prophylaxis of angioedema attacks in adults and adolescents with documented diagnosis of hereditary angioedema.
- Patient must have a history of at least one severe event per month (documentation required).
- Patient has tried and failed or is intolerant to at least one other prior therapy, including 17 alpha-alkylated androgens (e.g. danazol, stanozolol) or an anti-fibrinolytic agent (e.g. tranexamic acid) for HAE prophylaxis (documentation required).

## DOSAGE/ADMINISTRATION:

- Prophylaxis of Hereditary angioedema:
  - Cinryze®: 1000 units IV infusion over 10 minutes every 3 to 4 days

- Safety and efficacy of Cinryze® have not been established in neonates, infants, or children

## PRECAUTIONS:

- Hypersensitivity reactions (e.g. hives, tightness of chest, wheezing, hypotension and anaphylaxis) may occur during or after injection; exercise caution for treatment choice as hypersensitivity reactions may be similar to symptoms of angioedema, epinephrine should be immediately available for acute hypersensitivity
- Thrombosis has been reported with off-label high doses
- Transmission of infectious agents, viruses, or Creutzfeldt-Jakob disease may occur; C1 esterase inhibitor is made from human blood

## Billing/Coding information

### Associated HCPCS Codes:

J0598	Injection, C1 esterase inhibitor (human), Cinryze, 10 units

### Associated CPT Coding:

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### Associated ICD-9 Coding:

277.6	Other deficiencies of circulating enzymes

## COST

AWP (November 2011)

- Cinryze®: \$50.04/ 10 units; \$5004.00/dose

## COMMITTEE APPROVAL:

## GUIDELINE UPDATE INFORMATION:


## REFERENCES:

- DRUGDEX®, accessed 11/3/11
- Product Information: Cinryze™ (C1 esterase inhibitor) for IV injection. ViroPharma Biologics, Inc. Exton, PA 2011.