

### Clinical Pharmacy Program Guidelines for Cinryze

Program	Prior Authorization
Medication	Cinryze <sup>®</sup> (C1 esterase inhibitor, human)
Issue Date	3/2013
Pharmacy and Therapeutics Approval Date	7/2017
Effective Date	9/2017

#### 1. Background:

Cinryze is a plasma-derived C1 esterase inhibitor (human) indicated for routine prophylaxis against angioedema attacks in adolescent and adult patients with hereditary angioedema (HAE).<sup>1</sup> Clinical evidence also supports the use of Cinryze for the treatment of acute attacks of HAE.<sup>2</sup>

Prophylactic administration of antifibrinolytic agents (e.g., tranexamic acid) and/or synthetic attenuated androgens (e.g., danazol, stanozolol) has proven useful in reducing the frequency or severity of attacks. C1-INH will also reduce the frequency of attacks.<sup>4</sup> A recent meta-analysis found that androgen derivatives, antifibrinolytics, and C1-INH appeared to be effective in HAE prophylaxis, however, it is still undetermined which prophylactic therapy is better than another.<sup>3</sup>

#### 2. Coverage Criteria:

<p><b>A. Cinryze</b> will be approved based on <b>all</b> of the following criteria:</p> <ol style="list-style-type: none"> <li>1. Diagnosis of hereditary angioedema (HAE)<sup>1-3</sup></li> </ol> <p style="text-align: center;"><b>-AND-</b></p> <ol style="list-style-type: none"> <li>2. <b>One</b> of the following:           <ol style="list-style-type: none"> <li>a. <b>Both</b> of the following:               <ol style="list-style-type: none"> <li>(1) For prophylaxis against HAE attacks<sup>1</sup></li> </ol> <p style="text-align: center;"><b>-AND-</b></p> <ol style="list-style-type: none"> <li>(2) <b>One</b> of the following:</li> </ol> </li> </ol> </li> </ol>
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(a) For continuation of prior therapy

**-OR-**

(b) History of failure, contraindication, or intolerance of **one** of the following:

- i. 17-alpha alkylated androgen (e.g., danazol, oxandrolone)
- ii. Antifibrinolytics (e.g., aminocaproic acid, tranexamic acid)

**-OR-**

b. **Both** of the following:

(1) For treatment of acute HAE attacks<sup>2</sup> (off-label)

**-AND-**

(2) Not used in combination with other approved treatments for acute HAE attacks (e.g. Berinert, Firazyr, Kalbitor or Ruconest)

**Authorization of therapy will be issued for 12 months.**

### 3. References:

1. Cinryze [package insert]. Lexington, MA: ViroPharma Biologics, Inc.; December 2016.
2. Riedl MA, Hurewitz DS, Levy R, et al. Nanofiltered C1 esterase inhibitor (human) for the treatment of acute attacks of hereditary angioedema: an open-label trial. *Ann Allergy Asthma Immunol.* 2012 Jan;108(1):49-53.
3. Costantino G1, Casazza G, Bossi I, et al. Long-term prophylaxis in hereditary angio-oedema: a systematic review. *BMJ Open.* 2012 Jul 11;2(4).
4. Tse K1, Zuraw BL. Recognizing and managing hereditary angioedema. *Cleve Clin J Med.* 2013 May;80(5):297-308.

Program	Prior Authorization –Cinryze (C1 esterase inhibitor, human)
<b>Change Control</b>	
Date	Change
3/2013	New pharmacy/medical guideline
9/2014	<p>Cinryze: Changed prophylaxis “of” to “against” HAE attacks, changed history of failure, contraindication, or intolerance of “alkylated androgen (eg, danazol)” to “17-alpha alkylated androgen (eg, danazol, oxandrolone) or Antifibrinolytics (eg, aminocaproic acid, tranexamic acid)”, and added continuation of prior therapy for patients who are being treated prophylactically. For the off-label treatment indication, added “Not used in combination with other approved treatments for acute HAE attacks (eg, Berinert, Firzayr, Kalbitor or Ruconest).”</p> <p>Berinert: Added “Not used in combination with other approved treatments for acute HAE attacks (e.g. Firzayr, Kalbitor or Ruconest).”</p> <p>Added new criteria for Ruconest, a newly approved C1 esterase inhibitor (recombinant), mirroring Firzayr and Berinert, with an authorization duration of 12 months:</p> <ul style="list-style-type: none"> <li>• Diagnosis of HAE</li> <li>• For the treatment of acute HAE attacks</li> <li>• Not used in combination with other approved treatments for acute HAE attacks (eg, Berinert, Firzayr, or Kalbitor)</li> <li>• Prescribed by an immunologist, allergist, or rheumatologist</li> </ul>
7/2016	Updated clinical criteria to align with Employer and Individual medical necessity, except prescriber requirement. Cinryze, Berinert, Ruconest separated into individual policies to align with Employer and Individual. Updated policy to new template.
7/2017	Annual review. Updated references.