

<b>Policy Title:</b>	Cinryze (C1 esterase inhibitor [human]) (Intravenous)		
		<b>Department:</b>	PHA
<b>Effective Date:</b>	01/01/2020		
<b>Review Date:</b>	10/02/2019, 12/18/19		
<b>Revision Date:</b>	10/02/2019		

**Purpose:** To support safe, effective and appropriate use of Cinryze (C1 esterase inhibitor [human]).

**Scope:** Medicaid, Exchange, Medicare-Medicaid Plan (MMP)

**Policy Statement:**

Cinryze (C1 esterase inhibitor [human]) is covered under the Medical Benefit when used within the following guidelines. Use outside of these guidelines may result in non-payment unless approved under an exception process.

**Procedure:**

Coverage of Cinryze (C1 esterase inhibitor [human]) will be reviewed prospectively via the prior authorization process based on criteria below.

***Initial Criteria:***

- Authorization may be granted for treatment of acute hereditary angioedema (HAE) attacks in members 12 years of age or older when either of the following criteria is met:
  - Member has C1 inhibitor deficiency or dysfunction as confirmed by laboratory testing; AND
  - Member has normal C1 inhibitor as confirmed by laboratory testing and meets one of the following criteria:
    - Member has an F12, angiotensin-1, or plasminogen gene mutation as confirmed by genetic testing, OR
    - Member has a family history of angioedema and the angioedema was refractory to a trial of high-dose antihistamine (e.g., cetirizine) for at least one month.
- The following documentation must be submitted with the initial request:
  - Laboratory report with C4 level, C1 inhibitor antigenic protein level and/or C1 inhibitor functional activity; AND
  - For the diagnosis of HAE with normal C1 inhibitor, F12 gene mutation testing results (if applicable)

***Continuation of Therapy Criteria:***

- Patient continues to meet initial criteria; AND
- Patient has experienced reduction in severity and duration of attacks since starting treatment; AND
- Documentation supporting a positive clinical response to therapy with Cinryze (e.g., chart notes, medical records)

**Coverage durations:**

- Initial coverage: 6 months
- Continuation of therapy coverage: 6 months

\*\*\* Requests will also be reviewed to National Coverage Determination (NCD) and Local Coverage Determinations (LCDs) if applicable.\*\*\*

**Dosage/Administration:**

Indication	Dose	Maximum dose (1 billable unit = 10 units )
HAE	<p><u>Adult/adolescents (<math>\geq 12</math> years old):</u></p> <ul style="list-style-type: none"> <li>• 1,000 units by intravenous injection every 3 to 4 days</li> </ul> <p>For patients who have not responded adequately to initial dosing, doses up to 2,500 U (not exceeding 100 U/kg) every 3 or 4 days may be considered based on individual patient response.</p> <p><u>Pediatric patients (6 to 11 years old):</u></p> <ul style="list-style-type: none"> <li>• 500 units by intravenous injection every 3 to 4 days</li> </ul> <p>The dose may be adjusted according to individual patient response, up to 1,000 U every 3 to 4 days.</p>	1,000 billable units per 30 days

**Investigational use:** All therapies are considered investigational when used at a dose or for a condition other than those that are recognized as medically accepted indications as defined in any one of the following standard reference compendia: American Hospital Formulary Service Drug information (AHFS-DI), Thomson Micromedex DrugDex, Clinical Pharmacology, Wolters Kluwer Lexi-Drugs, or Peer-reviewed published medical literature indicating that sufficient evidence exists to support use. Neighborhood does not provide coverage for drugs when used for investigational purposes.

### Applicable Codes:

Below is a list of billing codes applicable for covered treatment options. The below tables are provided for reference purposes and may not be all inclusive. Requests received with codes from tables below do not guarantee coverage. Requests must meet all criteria provided in the procedure section.

The following HCPCS/CPT codes are:

HCPCS/CPT Code	Description
J0598	Injection, C1 esterase inhibitor (human), Cinryze, 10 units

### References:

1. Cinryze [package insert]. Lexington, MA: ViroPharma Biologics; June 2018.
2. Maurer M, Magerl M, Ansotegui I, et al. The international WAO/EAACI guideline for the management of hereditary angioedema – the 2017 revision and update. *Allergy*. 2018;00:1-22.
3. Cicardi M, Bork K, Caballero T, et al. Hereditary Angioedema International Working Group. 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.
6. Zuraw BL, Bork K, Binkley KE, et al. Hereditary angioedema with normal C1 inhibitor function: consensus of an international expert panel. *Allergy Asthma Proc*. 2012; 33(6):S145-S156.
7. Lang DM, Aberer W, Bernstein JA, et al. International consensus on hereditary and acquired angioedema. *Ann Allergy Asthma Immunol*. 2012; 109:395-202.
8. Cicardi M, Aberer W, Banerji A, et al. Classification, diagnosis, and approach to treatment for angioedema: consensus report from the Hereditary Angioedema International Working Group. *Allergy*. 2014;69: 602-616.

9. Bowen T. Hereditary angioedema: beyond international consensus – circa December 2010 – The Canadian Society of Allergy and Clinical Immunology Dr. David McCourtie Lecture. *Allergy Asthma Clin Immunol.* 2011;7(1):1.
10. Bernstein J. Update on angioedema: Evaluation, diagnosis, and treatment. *Allergy and Asthma Proceedings.* 2011;32(6):408-412.
11. Longhurst H, Cicardi M. Hereditary angio-edema. *Lancet.* 2012;379:474-481.
12. [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.