

Title: C1 inhibitor, human (Cinryze)

Origination: 08/26/09	Revised:	Annual Review: 12/15/11
------------------------------	-----------------	--------------------------------

Purpose:

To provide guidelines and criteria for the review and decision determination of requests for medications that requires prior authorization.

Background Information:

Reference Statement

- Guidelines will be compiled from available US Food and Drug Administration (FDA) approved indications, general practice guidelines, and/or evidence-based uses established through phase III clinical studies without published conflicting data. Only clinical studies published in their entirety in reputable peer-reviewed journals will be evaluated.

Medication Summary

- Cinryze (human C1 inhibitor) is a normal constituent of human blood that functions to inhibit the activation of the intrinsic coagulation, complement and fibrinolytic systems.
- Cinryze is used for the prevention of angioedema attacks in adolescents and adults with **hereditary angioedema (HAE)**. HAE is a very rare genetic disorder that presents as acute, recurrent attacks of soft tissue skin swelling, abdominal pain, and potentially life-threatening upper airway obstruction.
- Cinryze is supplied as 500 unit vials, and is administered as a 1000 unit (10ml) IV dose over at least 10 minutes every three (3) to four (4) days. One (1) unit of Cinryze corresponds to the mean quantity of C1 inhibitor present in 1ml of normal human plasma.

Eligibility Criteria

- Member must be eligible and have applicable benefits.
- Prior authorization requests that do not meet clinical criteria in this Procedure will be forwarded to a Clinical Pharmacist for review.

Exclusions

- Members less than six (6) years of age, as safety and efficacy have not been established.
- Cinryze is **not indicated** for the treatment of an acute angioedema attack.

Title: C1 inhibitor, human (Cinryze)

Procedure:

- 1.0 Request for *initial therapy for short-term or long-term prophylaxis only (not indicated for acute treatment)* for **Hereditary Angioedema (HAE)** requires documentation from the Member's medical records maintained by the requesting independent practitioner verifying the following:
 - 1.1 Provider must be an allergist or immunologist; **AND**
 - 1.2 Diagnosis of Hereditary Angioedema (copy of lab report, C4 and C1-inhibitor assays, with reference ranges is required); **AND**
 - 1.3 Member's history of HAE attacks is consistent with at least **ONE** (1) of the following criteria:
 - 1.3.1 Has more than one (1) severe event (respiratory or abdominal attack) per month;
 - 1.3.2 Is disabled for more than five (5) days per month due to severity of attacks;
 - 1.3.3 Has experienced a laryngeal attack (airway obstruction);
 - 1.4 Member is **NOT** concurrently taking estrogen therapy (hormone replacement or contraceptives) **OR** an angiotensin converting enzyme (ACE) inhibitor (these medications are well know triggers for attacks and should be avoided);
 - 1.5 Member has had an inadequate response, after confirmed adherence to therapy, with attenuated androgens (danazol or oxandrolone);
- OR**
- 1.5 Member has one (1) of the following contraindications to the use of attenuated androgens (danazol or oxandrolone):
 - 1.5.1 Pregnancy and lactation;
 - 1.5.2 Breast cancer;
 - 1.5.3 Prostate cancer;
 - 1.5.4 Children when long-term use is expected (androgens are used in children for short-term prophylaxis);
 - 1.5.5 Severe cardiac disease;
 - 1.5.6 Severe renal failure;
 - 1.5.7 Severe hepatic disease;
 - 1.5.8 Acute porphyria;

Title: C1 inhibitor, human (Cinryze)

Procedure, continued:

1.0 Request for *initial therapy for short-term or long-term prophylaxis only (not indicated for acute treatment)* for **Hereditary Angioedema (HAE)** requires documentation from the Member's medical records maintained by the requesting independent practitioner verifying the following (continued):

OR

1.5 Member has had **one (1) or more** of the following adverse effects or an intolerance to the use of attenuated androgens (danazol or oxandrolone):

1.5.1 Elevated serum transaminases not improved by dose reduction (ALT, AST - liver enzymes);

1.5.2 Androgenic effects, such as significant weight gain, acne vulgaris, seborrhea, hirsutism, virilization, alopecia, deepening of the voice, pharyngitis, hoarseness;

1.5.3 Menstrual irregularities;

1.5.4 Intracranial hypertension (manifested as headaches, papilledema, nausea/vomiting, and visual impairment);

1.5.5 Allergic reactions (manifested by urticaria, pruritus, maculopapular rash, Stevens-Johnson syndrome);

1.5.6 Thrombotic events (myocardial infarction, stroke);

1.6 If the Member meets all the above criteria, initial therapy for Cinryze may be approved for up to three (3) months at a dose of 1000 units (10ml) given IV every three (3) to four (4) days (2 doses per week).

2.0 Request for *continuation of therapy* beyond the initial authorization period for **Hereditary Angioedema (HAE)** requires documentation from the Member's medical records maintained by the requesting independent practitioner verifying there has been a significant reduction (50% or greater) in the number of angioedema attacks from baseline:

2.1 If the Member meets the above criteria, continuation of therapy with Cinryze may be approved for up to six (6) months at a dose of 1000 units (10ml) given IV every three (3) to four (4) days (2 doses per week).

Title: C1 inhibitor, human (Cinryze)

References:

1. Cinryze (C1Esterase Inhibitor [Human]) Prescribing information. VioPharma Incorporated. Lev Pharmaceuticals, Inc. New York, NY. <http://www.cinryze.com/> Accessed June 2009
2. Atkinson, John P et al. "Prevention of attacks in hereditary angioedema." *Up To Date*. Last literature review version 17.1: January 2009 | This topic last updated: February 17, 2009
3. Atkinson, John P et al. "Diagnosis of hereditary and acquired angioedema (C1 inhibitor disorders)." *Up To Date*. Last literature review version 17.1: January 2009 | This topic last updated: June 13, 2008
4. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2008. Available at: <http://cp.gsm.com>.
5. Farkas, Henriette et al. "Management of Hereditary Angioedema in Pediatric Patients." *Pediatrics*. 2007;120:e713-e722.
6. Epstein T and Bernstein J. "Current and Emerging Management Options for Hereditary Angioedema in the US." *Drugs*. 2008;68 (18): 2561-2573.

Disclaimer Information:

Prior Authorization criteria are developed to determine coverage for AvMed Health Plans' benefits, and are published to provide a better understanding of the basis upon which coverage decisions are made. AvMed Health Plans makes coverage decisions based on the Member's benefit plan contract and these criteria. This guideline sets forth concise clinical coverage criteria which have been developed from a review of current literature, policies of the FDA and other government agencies, and other appropriate references, in consultation and with approval from practicing physicians who are members of AvMed's Pharmacy and Therapeutic committee. Treating providers are solely responsible for the medical advice and treatment of Members. This guideline may be updated and therefore is subject to change. The use of these criteria is neither a guarantee of payment nor a final prediction of how specific claim(s) will be adjudicated.