

Drug Policy

Policy:	201006	Initial Effective Date:
Code(s):	HCPCS J0598, J0599	12/21/2010
SUBJECT:	Cinryze® (C1 esterase inhibitor) Haegarda® (C1 esterase inhibitor)	Annual Review Date: 03/19/2024
		Last Revised Date: 03/19/2024

Subject to Site of Care

Prior approval is required for some or all procedure codes listed in this Corporate Drug Policy.

Initial and renewal requests for the medication(s) listed in this policy are subject to site of care management. When billed under the medical benefit, administration of the medication will be restricted to a non-hospital facility-based location (i.e., home infusion provider, provider’s office, free-standing ambulatory infusion center) unless the member meets the site of care exception criteria. To view the exception criteria and a list of medications subject to site of care management please [click here](#).

OVERVIEW

Cinryze and Haegarda are human plasma-derived C1-INH indicated for routine prophylaxis against angioedema attacks in adolescent and adult patients with hereditary angioedema (HAE). The safety and efficacy of Cinryze or Haegarda for the treatment of acute attacks have not been established.

Hereditary angioedema is a rare, debilitating, potentially life-threatening genetic disorder caused by a deficiency in C1-INH, a plasma protein involved in the regulation of the complement and intrinsic coagulation pathways. Hereditary angioedema is caused by mutations in the C1-INH gene located on chromosome 11q and inherited as an autosomal dominant trait. Two main types of hereditary angioedema exist: mutations causing Type I hereditary angioedema are associated with decreased production of C1-INH leading to decreased functional levels; Type II hereditary angioedema mutations are associated with a dysfunctional C1 inhibitor, but the inhibitor level is normal.

HAE is characterized by recurrent episodes of nonpruritic, nonpitting, subcutaneous or submucosal edema associated with pain syndrome, nausea, vomiting, diarrhea, and/or life-threatening airway swelling. Airway obstruction due to swelling is life-threatening if left untreated. There is a wide variation in the frequency and severity of attacks. Clinical experience suggests that minor trauma and/or stress, among other triggers, may precipitate attacks. Untreated attacks typically last over 48 to 96 hours. Short-term prophylaxis with a C1-INH - is recommended if more than minor manipulation (e.g., mild dental work) is needed, and prior to intubation or major procedures. The dose for short-term prophylaxis with C1-INH varies from 10 U/kg to 20 U/kg or 1,000 units, 1 to 6 hours before procedure. Long-term prophylaxis should be considered in all severely symptomatic patients, taking into consideration the severity of disease, frequency of attacks, patient’s quality of life, availability of resources, and failure to achieve adequate control by on-demand therapy.

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POLICY STATEMENT

This policy involves the use of Cinryze and Haegarda. Prior authorization is recommended for pharmacy and medical benefit coverage of Cinryze and Haegarda. Approval is recommended for those who meet the conditions of coverage in the **Criteria, Dosing (medical benefit requests only), Initial/Extended Approval, Duration of Therapy, and Labs/Diagnostics** for the diagnosis provided. **Waste Management** applies for all covered conditions that are administered by a healthcare professional. **Conditions Not Recommended for Approval** are listed following the recommended authorization criteria and Waste Management section. Requests for uses not listed in this policy will be reviewed for evidence of efficacy and for medical necessity on a case-by-case basis.

Because of the specialized skills required for evaluation and diagnosis of patients treated with Cinryze and Haegarda as well as the monitoring required for AEs and long-term efficacy, initial approval requires Cinryze and Haegarda be prescribed by or in consultation with a physician who specializes in the condition being treated. All approvals for initial therapy are provided for the initial approval duration noted below; if reauthorization is allowed, a response to therapy is required for continuation of therapy unless otherwise noted below.

The site of care medical necessity criteria applies to initial therapy and reauthorizations under the medical benefit only.

Medical Necessity:

Coverage will be provided when the following criteria have been met:

The requested medication will not be used Concomitantly with Other HAE Prophylactic Therapies (e.g. Cinryze, Haegarda, Takhzyro). Cinryze and Haegarda have not been studied in combination with other prophylactic therapies for HAE, and combination therapy for long-term prophylactic use is not recommended; AND

The requested medication will not be used for acute treatment of hereditary angioedema attacks. The Company considers Cinryze or Haegarda for acute treatment of hereditary angioedema attacks investigational and not eligible for reimbursement; AND

1. Hereditary Angioedema (HAE) Type 1 and 2 Prophylaxis, Initial Therapy

Criteria. *Patient must meet the following criteria (A, B, C, D, E, F, G, H, and I):*

- A.** The patient has HAE as confirmed by following criteria (a or b)
 - a.** Patient has low levels of functional C1-INH protein (< 50% of normal) as defined by the laboratory reference values [documentation required]; OR
 - b.** Patient has lower than normal serum C4 levels (< 14 mg/dL), as defined by the laboratory reference values AND lower than normal C1-INH level (< 19.9 mg/dL) [documentation required]; AND
- B.** The medication is prescribed by or in consultation with an allergist, immunologist, hematologist or a physician that specializes in the treatment of HAE or related disorders; AND
- C.** All other causes of acquired angioedema (e.g., medications, auto-immune diseases) have been excluded; AND
- D.** Patient has at least ONE of the following criteria (a, b, or c)

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- a. Patient has a history of one or more severe attack(s) per month (defined as an attack that significantly interrupts daily activities despite short-term treatment); OR
- b. Disabling symptoms for at least 5 days per month; OR
- c. Laryngeal edema; AND
- E. Patient has at least ONE of the following criteria (a, b, or c); AND
 - a. Patient must have history of self-limiting, non-inflammatory subcutaneous angioedema, without urticaria, which is recurrent and lasts >12 hours; OR
 - b. Self-limiting, recurrent abdominal pain without a clear organic cause lasting >6 hours; OR
 - c. A history of laryngeal edema; AND
- F. Cinryze and Haegarda are not used in combination with other approved treatments for HAE (e.g. Firazyr, Berinert, Kalbitor, or Ruconest); AND
- G. If the requested drug is Cinryze or Haegarda, the patient is 6 years of age or older; AND
- H. Site of care medical necessity is met*.

2. Patient has been started on Cinryze or Haegarda

Criteria. *Patient must meet the following criteria (A, B, C, D, E, F, G, H, I, J, K, and L):*

- A. The patient has HAE as confirmed by following criteria (a or b):
 - a. Patient has low levels of functional C1-INH protein (< 50% of normal) as defined by the laboratory reference values [documentation required]; OR
 - b. Patient has lower than normal serum C4 levels (< 14 mg/dL or as defined by the laboratory reference values) AND lower than normal C1-INH level (< 19.9 mg/dL or as defined by the laboratory reference values) [documentation required]; AND
- B. The medication is prescribed by or in consultation with an allergist, immunologist, hematologist or a physician that specializes in the treatment of HAE or related disorders; AND
- C. All other causes of acquired angioedema (e.g., medications, auto-immune diseases) have been excluded; AND
- D. Patient has at least ONE of the following:
 - a. Patient has a history of one or more severe attack(s) per month (defined as an attack that significantly interrupts daily activities despite short-term treatment); OR
 - b. Disabling symptoms for at least 5 days per month; OR
 - c. Laryngeal edema; AND
- E. Patient has at least ONE of the following criteria:
 - a. Patient must have history of self-limiting, non-inflammatory subcutaneous angioedema, without urticaria, which is recurrent and lasts >12 hours; OR
 - b. Self-limiting, recurrent abdominal pain without a clear organic cause lasting >6 hours; OR
 - c. A history of laryngeal edema; AND
- F. Cinryze and Haegarda are not used in combination with other approved treatments for HAE (e.g. Firazyr, Berinert, Kalbitor, or Ruconest); AND
- G. Patient has at least 1 annual assessment by an HAE specialist; AND
- H. The patient has had a favorable clinical response (e.g. decrease in the duration of HAE attacks, quick onset of symptom relief, complete resolution of symptoms, decrease in HAE attack frequency or severity); AND

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- I. Reduction in the utilization of on-demand therapies used for acute attacks (e.g. Berinert, Ruconest, Firazyf, Kalbitor) as determined by claims information, while on Cinryze/Haegarda therapy; AND
- J. If the requested drug is Cinryze or Haegarda, the patient is 6 years of age or older; AND
- K. Site of care medical necessity is met*

Dosing in Cinryze and Haegarda. *Dosing must meet the following:*

Cinryze: IV:

12 years of age and older: 1,000 units every 3 to 4 days; doses $\leq 2,500$ units (≤ 100 units/kg) every 3 or 4 days may be considered based on individual patient response.

Children 6 to 11 years: IV: 500 units every 3 to 4 days; adjust dose based on individual patient response, up to 1,000 units every 3 to 4 days

Haegarda: SubQ: 60 units/kg every 3 or 4 days.

Initial Approval/ Extended Approval.

A) *Initial Approval:* 1 year

B) *Extended Approval:* 1 year

Documentation Requirements:

The Company reserves the right to request additional documentation as part of its coverage determination process. The Company may deny reimbursement when it has determined that the drug provided or services performed were not medically necessary, investigational or experimental, not within the scope of benefits afforded to the member and/or a pattern of billing or other practice has been found to be either inappropriate or excessive. Additional documentation supporting medical necessity for the services provided must be made available upon request to the Company.

Documentation requested may include patient records, test results and/or credentials of the provider ordering or performing a service. The Company also reserves the right to modify, revise, change, apply and interpret this policy at its sole discretion, and the exercise of this discretion shall be final and binding.

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Edits and Denials:

Prior approval: Prior approval is required for Cinryze (**HCPCS Code J0598**) or Haegarda (**HCPCS Code J0599**). Requests for prior approval will be authorized by a nurse reviewer if submitted documentation meets criteria outlined within Corporate Medical Policy.

Requests for prior approval will be forwarded to a qualified physician consultant for review if submitted documentation does not meet criteria outlined within Corporate Medical Policy.

TOPPS: Claims received with **HCPCS Code J0598 or J0599** will edit with **Remark Code M3M or M4M M6J** and adjudicated in accordance with the Corporate Medical Policy.

Appeals: Appeals submitted to Medical Review will be approved by a nurse reviewer if documentation meets criteria outlined within Corporate Medical Policy.

Appeals submitted to Medical Review will be forwarded to the Chief Medical Officer or specialty matched physician consultant for review if documentation does not meet criteria outlined within Corporate Medical Policy.

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Liability: A participating provider will be required to write off charges denied as not medically necessary.

HCPCS Code(s):	
J0598	Injection, C-1 esterase inhibitor (human), Cinryze, 10 units
J0599	Injection, c-1 esterase inhibitor (human), Haegarda, 10 units

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