# PRIOR AUTHORIZATION POLICY

**POLICY:** Hereditary Angioedema – C1 Esterase Inhibitors (Subcutaneous) Prior Authorization Policy
- Haegarda® (C1 esterase inhibitor [human] for subcutaneous [SC] use – CSL Behring)

**REVIEW DATE:** 08/26/2020

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## OVERVIEW

Haegarda is a C1 esterase inhibitor (C1-INH) replacement therapy for hereditary angioedema (HAE).[1] It is a human plasma-derived C1-INH and is indicated for routine prophylaxis to prevent HAE attacks in adults and pediatric patients ≥ 6 years of age.[1]

### Disease Overview

HAE due to C1-INH deficiency has two subtypes: HAE type I and HAE type II. HAE diagnosis can be confirmed by measuring functional C1-INH protein levels (usually < 50% of normal in patients with HAE), C4 levels, and C1-INH antigenic levels.[2,3] Patients with HAE type I have low C4 and C1-INH antigenic protein levels, along with low levels of functional C1-INH protein. Patients with HAE type II have low C4 and functional C1-INH protein level, with a normal or elevated C1-INH antigenic protein level. C1-INH replacement therapies are appropriate for both HAE type I and type II.

Patients with the third type of HAE called HAE with normal C1-INH (HAE nC1-INH), previously referred to as HAE type III, have normal C4 and C1-INH antigenic protein levels.[2] HAE nC1-INH is much less prevalent than HAE types I/II, and the exact cause of HAE nC1-INH has not been determined.[2,4] Pathogenic variants in the genes encoding for Factor XII (regulates bradykinin generation), angiopoietin-1 (involved in vascular permeability), and plasminogen have been associated with HAE nC1-INH; however, the majority of cases have unknown etiology. There are no randomized or controlled clinical trial data available with any therapy for use in HAE nC1-INH.[4-6]

### Guidelines

According to international/Canadian guidelines (updated 2019), the decision to initiate long-term prophylaxis is individualized based on multiple factors and should be made by the patient and an HAE specialist.[4] C1-INH concentrate and Takhzyro™ (lanadelumab-flyo injection) are recognized as treatment options for long-term prophylaxis of HAE type I/II attacks.[3,4] Androgens are not considered first-line and are contraindicated in certain groups (e.g., pregnancy, prepubescent children, androgen-dependent malignancy).[4] In other populations, the use of androgens for long-term prophylaxis may be considered as second-line but should be considered critically due to potential for adverse events. Therefore, guidelines note that androgens should not be used in patients who have a preference for alternative therapy and that patients should not be required to fail anabolic androgen therapy as a prerequisite to receiving prophylactic C1-INH or Takhzyro therapy.[4,7]

## POLICY STATEMENT

Prior authorization is recommended for prescription benefit coverage of Haegarda. Because of the specialized skills required for evaluation and diagnosis of patients treated with Haegarda, approval requires Haegarda to be prescribed by or in consultation with a physician who specializes in the condition being treated. All approvals are provided for the duration noted below.

**Documentation:** Documentation will be required where noted in the criteria as **[documentation required]**. Documentation may include, but is not limited to, chart notes, laboratory records, and prescription claims records.

**Automation:** None.

## RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Haegarda is recommended in those who meet the following criteria:

### FDA-Approved Indications

1. **Hereditary Angioedema (HAE) Due to C1 Inhibitor (C1-INH) Deficiency [Type I or Type II] – Prophylaxis.** Approve Haegarda for the duration noted if the patient meets one of the following criteria (A or B):
   - **A)** Initial therapy. Approve for 1 year if the patient meets both of the following criteria (i and ii):
     - **i.** Patient has HAE type I or type II as confirmed by the following diagnostic criteria (a and b):
       - **a)** Patient has low levels of functional C1-INH protein (< 50% of normal) at baseline, as defined by the laboratory reference values **[documentation required]**; AND
       - **b)** Patient has lower than normal serum C4 levels at baseline, as defined by the laboratory reference values **[documentation required]**; AND
     - **ii.** The medication is prescribed by or in consultation with an allergist/immunologist or a physician who specializes in the treatment of HAE or related disorders.
   - **B)** Patients currently receiving Haegarda prophylaxis. Approve for 1 year if the patient meets all of the following criteria (i, ii, and iii):
     - **i.** Patient has a diagnosis of HAE type I or II **[documentation required]**; AND
     - **ii.** According to the prescriber, the patient has had a favorable clinical response since initiating Haegarda prophylactic therapy compared with baseline (i.e., prior to initiating prophylactic therapy); AND
       Note: Examples of favorable clinical response include decrease in HAE acute attack frequency, decrease in HAE attack severity, or decrease in duration of HAE attacks.
     - **iii.** The medication is prescribed by or in consultation with an allergist/immunologist or a physician who specializes in the treatment of HAE or related disorders.

## CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Haegarda is not recommended in the following situations:

1. **Concomitant Use with Other HAE Prophylactic Therapies (e.g., Cinryze®, Takhzyro™).** Haegarda has not been studied in combination with other prophylactic therapies for HAE, and combination therapy for long-term prophylactic use is not recommended. Patients may use other medications, including Cinryze, for treatment of acute HAE attacks, and for short-term (procedural) prophylaxis.

2. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

## REFERENCES

1. Haegarda® subcutaneous injection [prescribing information]. Kankakee, IL: CSL Behring LLC; September 2020.

2. Bowen T, Cicardi M, Farkas H, et al. 2010 international consensus algorithm for the diagnosis, therapy and management of hereditary angioedema. *Ann Allergy Asthma Immunol*. 2010;6:24.
3. Mauer 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;73(8):1575-1596. Available at: https://onlinelibrary.wiley.com/doi/epdf/10.1111/all.13384. Accessed on August 4, 2020.
4. Betschel S, Badiou J, Binkley K, et al. The International/Canadian Hereditary Angioedema Guideline [published correction appears in Allergy Asthma Clin Immunol. 2020 May 6;16:33]. *Allergy Asthma Clin Immunol*. 2019;15:72. Available at: https://aacijournal.biomedcentral.com/articles/10.1186/s13223-019-0376-8. Accessed on August 4, 2020.
5. 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:S145-S156.
6. Magerl M, Germenis AE, Maas C, et al. Hereditary angioedema with normal C1 inhibitor. Update on evaluation and treatment. *Immunol Allergy Clin N Am*. 2017;37:571-584.
7. 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;1:458-467. Available at: https://haei.org/wp-content/uploads/2015/04/Zuraw-B-L-US-HAEA-MAB-2013-Recommendations.pdf. Accessed on August 4, 2020.