VENTURA COUNTY
HEALTH CARE PLAN

PRIOR AUTHORIZATION POLICY

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

TAC APPROVAL DATE: 08/07/2019

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 against angioedema attacks in adolescent and adult patients with HAE.

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, currently called HAE with normal C1-INH (previously referred to as HAE type III), have normal C4 and C1-INH antigenic protein levels.[4] The exact cause of HAE with normal C1-INH has not been determined. There are no randomized or controlled clinical trial data available with any therapy for use in HAE with normal C1-INH.[4,5] Until data from randomized controlled studies become available, no firm recommendations regarding the treatment of HAE with normal C1-INH can be made.[4]

Guidelines

Per the World Allergy Organization/European Academy of Allergy and Clinical Immunology guidelines (2017), C1-INH concentrate is first-line for long-term prophylaxis.[3] Androgens should not be used in pregnant or breastfeeding women, or in children < 16 years of age. 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, the US Hereditary Angioedema Association Medical Advisory Board's position (2013) is that anabolic 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 therapy.[6] Plasma-derived C1-INH therapy has been proven to be effective and safe for long-term prophylactic therapy. Of note, these guidelines have not been updated to include Takhzyro™ (lanadelumab-flyo injection).

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.** The 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 is currently receiving Haegarda for HAE type I or type II prophylaxis [documentation required to confirm HAE type I or type II diagnosis]; AND
     - **ii.** According to the prescriber, the patient has had a favorable clinical response (e.g., decrease in number of HAE acute attack frequency, decrease in HAE attack severity, decrease in duration of HAE attacks) since initiating Haegarda prophylactic therapy compared with baseline (i.e., prior to initiating prophylactic therapy); AND
     - **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 has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval.).

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; October 2017.

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 1, 2019.
4. 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.
5. 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.
6. 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 1, 2019.

HISTORY

Type of Revision	Summary of Changes*	TAC Approval Date
Annual revision	New policy	08/02/2017
Selected revision	Added "Due to C1 Inhibitor (C1-INH) Deficiency [Type I or Type II]" to HAE indication description. Added documentation requirement for initial therapy laboratory diagnostic criteria and to confirm diagnosis in patients continuing therapy. Added criteria confirming favorable clinical response for patients continuing therapy.	11/15/2017
Annual revision	No criteria changes	08/01/2018
Selected revision	**Concomitant use with other HAE prophylactic therapies:** Added to conditions not recommended for approval. **All Indications:** Approval duration decreased to 1 year from 3 years.	10/03/2018
Annual revision	**All Indications:** "Prescribing physician" changed to "prescriber" throughout policy.	08/07/2019

TAC – Therapeutic Assessment Committee; * For a further summary of criteria changes, refer to respective TAC minutes available at: http://esidepartments/sites/Dep043/Committees/TAC/Forms/AllItems.aspx.