C1 Esterase Inhibitor Subcutaneous (Human) (Haegarda®)

NDC CODE(S) 63833-0828-XX HAEGARDA 2000UNIT Solution Reconstituted (CSL BEHRING, LLC))
63833-0829-XX HAEGARDA 3000UNIT Solution Reconstituted (CSL BEHRING, LLC)

DESCRIPTION

On March 28, 2017, the FDA approved the first subcutaneous C1 Esterase Inhibitor for the prevention of Hereditary Angioedema (HAE) attacks. Haegarda® is a human plasma-derived concentrate of C1 Esterase Inhibitor (Human) (C1-INH) indicated for routine prophylaxis to prevent Hereditary Angioedema (HAE) attacks in adolescent and adult patients. Haegarda® is prepared from large pools of human plasma from U.S. donors and is a purified, pasteurized, lyophilized concentrate of C1-INH to be reconstituted for subcutaneous administration. The potency of C1-INH is expressed in International Units (IU), which is related to the current WHO Standard for C1-INH products.

HAE patients have absence or low levels of endogenous or functional C1-INH. Although the events that cause attacks of angioedema in HAE patients are not well defined, it is theorized that increased vascular permeability and the clinical manifestation of HAE attacks may be primarily mediated through contact system activation. Suppression of contact system activation by C1-INH through the inactivation of plasma kallikrein and factor XIIa is thought to modulate vascular permeability by preventing the generation of bradykinin. Administration of Haegarda® replaces the missing or malfunctioning C1-INH protein in patients with HAE.

POLICY

- C1 Esterase Inhibitor Subcutaneous (Human) (Haegarda®) for the prevention of Hereditary Angioedema (HAE) attacks is considered ***medically necessary*** if the medical appropriateness criteria are met. **(See Medical Appropriateness below.)**
- C1 Esterase Inhibitor Subcutaneous (Human) (Haegarda®) for the treatment of other conditions/diseases is considered investigational.

MEDICAL APPROPRIATENESS

INITIAL APPROVAL

- C1 Esterase Inhibitor Subcutaneous (Human) (Haegarda®) for the prevention of Hereditary Angioedema (HAE) attacks is considered **medically appropriate** if **ALL** of the following criteria are met:
  - Individual is 6 years of age or older
  - Not used in combination with other prophylactic therapies targeting C1 inhibitor or kallikrein (e.g., Cinryze® or Takhzyro™)
  - Confirmation individual is avoiding **ALL** of the following possible triggers for HAE attacks:
    - Estrogen-containing agents including oral contraceptives AND hormone replacement therapy
    - Antihypertensive agents containing ACE inhibitors
    - Dipeptidyl peptidase IV (DPP-IV) inhibitors (e.g., sitagliptin)
    - Neprilysin inhibitors (e.g., sacubitril)
  - Individual has a history of **ANY ONE** of the following criteria for long-term HAE prophylaxis:
    - History of two (2) or more severe HAE attacks per month (e.g., airway swelling, debilitating cutaneous or gastrointestinal episodes)
    - Disabled more than 5 days per month by HAE
    - History of at least one laryngeal attack caused by HAE
  - Treatment with "on-demand" therapy (i.e., Kalbitor®, Firazyr®, Ruconest®, or Berinert®) did not provide satisfactory control or access to "on-demand therapy" is limited

- Individual has **ANY ONE** of the following clinical presentations consistent with a HAE subtype, which must be confirmed by repeat blood testing (treatment for acute attack should not be delayed for confirmatory testing):
  - **HAE I (C1-Inhibitor deficiency)** with **ALL** of the following:
    - Low C1 inhibitor (C1-INH) antigenic level (C1-INH antigenic level below the lower limit of normal as defined by the laboratory performing the test)
    - Low C4 level (C4 below the lower limit of normal as defined by the laboratory performing the test)
    - Low C1-INH functional level (C1-INH functional level below the lower limit of normal as defined by the laboratory performing the test) and **ANY ONE** of the following:
      - Individual has a positive family history of HAE
      - Acquired angioedema has been ruled out (i.e., onset of symptoms occur prior to 30 years old, normal C1q levels, individual does not have underlying disease such as lymphoma or benign monoclonal gammopathy [MGUS], etc.)
  - **HAE II (C1-Inhibitor dysfunction)** with **ALL** of the following:
    - Normal to elevated C1-INH antigenic level
    - Low C4 level (C4 below the lower limit of normal as defined by the laboratory performing the test)
    - Low C1-INH functional level (C1-INH functional level below the lower limit of normal as defined by the laboratory performing the test)
  - **HAE with normal C1-INH (formerly known as HAE III),** Prophylaxis for HAE with normal C1-INH is not routinely recommended and will be evaluated on a case by case basis

RENEWAL CRITERIA

- C1 Esterase Inhibitor Subcutaneous (Human) (Haegarda®) is considered **medically appropriate** for renewal if **ALL** of the following criteria are met:
  - Individual continues to meet initial approval criteria
  - Significant improvement in severity and duration of attacks have been achieved and sustained
  - Absence of unacceptable toxicity from the drug, Examples of unacceptable toxicity include the following: severe hypersensitivity reactions, thromboembolic events, etc.

INDICATION(S)	DOSAGE & ADMINISTRATION
Prophylaxis of Hereditary Angioedema (HAE) attacks	60 IU/kg body weight injected subcutaneously twice weekly (every 3 or 4 days)

LENGTH OF AUTHORIZATION

Coverage will be provided for 12 months and may be renewed

Refer to **DOSAGE LIMITS** below

APPLICABLE TENNESSEE STATE MANDATE REQUIREMENTS

BlueCross BlueShield of Tennessee's Medical Policy complies with Tennessee Code Annotated Section 56-7-2352 regarding coverage of off-label indications of Food and Drug Administration (FDA) approved drugs when the off-label use is recognized in one of the statutorily recognized standard reference compendia or in the published peer-reviewed medical literature.

IMPORTANT REMINDER

We develop Medical Policies to provide guidance to Members and Providers. This Medical Policy relates only to the services or supplies described in it. The existence of a Medical Policy is not an authorization, certification, explanation of benefits or a contract for the service (or supply) that is referenced in the Medical Policy. For a determination of the benefits that a Member is entitled to receive under his or her health plan, the Member's health plan must be reviewed. If there is a conflict between the Medical Policy and a health plan, the express terms of the health plan will govern.

ADDITIONAL INFORMATION

For appropriate chemotherapy regimens, dosage information, contraindications, precautions, warnings, and monitoring information, please refer to one of the standard reference compendia (e.g., the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) published by the National Comprehensive Cancer Network®, Drugdex Evaluations of Micromedex Solutions at Truven Health, or The American Hospital Formulary Service Drug Information).

SOURCES

Betschel, S., Badiou, J., Binkley, K., Borici-Mazi, R., Hébert, J., Kanani, A., et al. (2019). The International/Canadian Hereditary Angioedema Guideline. Allergy, Asthma & Clinical Immunology. 2019. 15:72. Published online 2019 Nov 25. doi: 10.1186/s13223-019-0376-8.

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Lumry, W. R. (2018). Current and emerging therapies to prevent hereditary angioedema attacks. *American Journal of Managed Care,* 24 (14), S299-S307.

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U. S. Food and Drug Administration. (2020, September). Center for Biologics Evaluation and Research. *HAEGARDA® (C1 esterase inhibitor subcutaneous [human]).* Retrieved November 25, 2020, 2020 from: https://www.fda.gov/downloads/BiologicsBloodVaccines/BloodBloodProducts/ApprovedProducts/LicensedProductsBLAs/FractionatedPlasmaProducts/UCM564335.

EFFECTIVE DATE 4/2/21

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