

Effective date: 7/1/2019
Reviewed Date: 6/2019, 9/2020, 2/2021, 2/2022, 3/2023, 12/2023, 01/2024, 07/2025, 11/2025, 06/2026
Pharmacy Scope: Medicaid
Medical Scope: Medicaid, Commercial, Medicare

SPECIALTY GUIDELINE MANAGEMENT

HAEGARDA (C1 Esterase Inhibitor Subcutaneous [Human])

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Routine prophylaxis to prevent Hereditary Angioedema (HAE) attacks in patients 6 years of age and older.

All other indications are considered experimental/investigational and are not a covered benefit.

II. SUMMARY OF EVIDENCE

Haegarda is a plasma-derived concentrate of C1 Esterase Inhibitor (Human) (C1-INH) indicated for routine prophylaxis to prevent Hereditary Angioedema (HAE) attacks in patients 6 years of age and older. HAE is a genetic disorder resulting from C1-INH deficiency, leading to excessive bradykinin-mediated swelling.

Approval of Haegarda is based on a randomized, double-blind, placebo-controlled, crossover trial in 90 patients aged 12 to 72 years with ≥ 4 attacks over a 2-month period. Patients were randomized to receive subcutaneous Haegarda at 40 IU/kg or 60 IU/kg twice weekly for 16 weeks, alternating with placebo. At the 60 IU/kg dose, Haegarda reduced the median number of attacks per month by 95% compared to baseline (0.5 vs. 4.0; $p < 0.001$), and by 83% versus placebo. The 40 IU/kg dose yielded a 72.8% reduction from baseline and 58% reduction versus placebo. Attack severity and duration were also reduced, and fewer patients required rescue medication during treatment. The most common adverse reactions ($\geq 4\%$) were injection site reactions, hypersensitivity (urticaria, pruritus), dizziness, and abdominal pain. No thromboembolic events, anaphylaxis, or viral transmissions were reported in clinical trials.

III. CRITERIA FOR APPROVAL

Authorization for 6 months may be granted for prevention of hereditary angioedema attacks when all of the following criteria is met:

- A. Member is ≥ 6 years of age.
- B. Medication is prescribed by, or in consultation with an allergist/immunologist or a physician who specializes in the management of HAE.
- C. Member has documented diagnosis of HAE type I or type II and meets one of the following (a or b):
 - a. Documentation that the member has C1 inhibitor deficiency or dysfunction as confirmed by laboratory testing; and meets one of the following criteria:

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- i. C1 inhibitor (C1-INH) antigenic level below the lower limit of normal as defined by the laboratory performing the test, or
 - ii. Normal C1-INH antigenic level and a low C1-INH functional level (functional C1-INH less than 50% or C1-INH functional level below the lower limit of normal as defined by the laboratory performing the test); OR
- b. Documentation that the member has normal C1 inhibitor as confirmed by laboratory testing and meets one of the following criteria:
 - i. Member has an F12, angiopoietin-1, plasminogen, or kininogen-1 (KNG1) gene, heparan sulfate-glucosamine 3-O-sulfotransferase 6 (HS3ST6), or myoferlin (MYOF) pathogenic variant as confirmed by genetic testing, or
 - ii. Member has a documented family history of angioedema and the angioedema was refractory to a trial of high-dose antihistamine (e.g., cetirizine 40mg per day or the equivalent) for at least one month.
- D. Other causes of angioedema have been ruled out (e.g., angiotensin-converting enzyme inhibitor [ACE-I] induced an angioedema, angioedema related to an estrogen containing drug, allergic angioedema).
- E. Member requires long-term prophylactic treatment based on the provider's assessment of the patient's disease activity, quality of life, availability of health care resources, and/or failure to achieve adequate control by appropriate on-demand therapy [i.e., Ekterly (sebetralstat), Kalbitor(ecallantide), Icatibant, Ruconest (C1 esterase inhibitor) or Berinert (C1 esterase inhibitor), etc.]
- F. Member will not use Haegarda (C1 esterase inhibitor), concomitantly with Takhzyro (lanadelumab-flyo), Andembry (garadacimab-gxii), Cinryze (C1 esterase inhibitor), Orladeyo (berotralstat) or Dawnzera (donidalorsen)
- G. Medicare members who have previously received this medication within the past 365 days are not subject to Step Therapy Requirements

IV. CONTINUATION OF THERAPY

Authorization of 6 months may be granted for continuation of therapy when all of the following criteria are met:

- A. Member meets all criteria for initial approval; AND
- B. Member has documentation of experiencing a significant reduction in frequency of attacks (e.g., $\geq 50\%$) since starting prophylactic treatment.; AND
- C. Member has documentation of reduced the use of medications to treat acute attacks since starting prophylactic treatment.

V. QUANTITY LIMIT

Haegarda 2000 units or 3000 units: 20 vials per 30 days (daily dose of 0.667)

Per §§ 42 CFR 422.101, this clinical medical policy only applies to Medicare in the absence of National Coverage Determination (NCD) or Local Coverage Determination (LCD).

Policy Rationale:

Haegarda was reviewed by the Neighborhood Health Plan of Rhode Island Pharmacy & Therapeutics (P&T) Committee. Neighborhood adopted the following clinical coverage criteria to ensure that its members use Haegarda according to Food

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and Drug Administration (FDA) approved labeling and/or relevant clinical literature. Neighborhood worked with network prescribers and pharmacists to draft these criteria. These criteria will help ensure its members are using this drug for a medically accepted indication, while minimizing the risk for adverse effects and ensuring more cost-effective options are used first, if applicable and appropriate. For Medicare members, these coverage criteria will only apply in the absence of National Coverage Determination (NCD) or Local Coverage Determination (LCD) criteria. Neighborhood will give individual consideration to each request it reviews based on the information submitted by the prescriber and other information available to the plan.

VI. DOSING AND ADMINISTRATION

Indication	Dose	Maximum dose (1 billable unit = 10 IU)
Prophylaxis of Hereditary Angioedema (HAE) attacks	60 IU/kg body weight injected subcutaneously twice weekly (every 3 or 4 days)	5,600 billable units per 28 days

The following HCPCS/CPT code is:

HCPCS/CPT Code	Description
J0599	Injection, c-1 esterase

VII. REFERENCES

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