CARECONTINUUM™

UTILIZATION MANAGEMENT MEDICAL POLICY

POLICY: Hereditary Angioedema – Andembry Utilization Management Medical Policy
- Andembry® (garadacimab subcutaneous injection – CSL Behring)

REVIEW DATE: 05/13/2026

OVERVIEW

Andembry, an activated Factor XII (FXIIa) inhibitor (monoclonal antibody), is indicated for **prophylaxis to prevent attacks of hereditary angioedema (HAE)** in adult and pediatric patients ≥ 12 years of age.[1]

Guidelines

According to US HAE Association Medical Advisory Board Guidelines (2020), when HAE is suspected based on clinical presentation, appropriate testing includes measurement of the serum C4 level, C1 esterase inhibitor (C1-INH) antigenic level, and C1-INH functional level.[2] Low C4 plus low C1-INH antigenic or functional level is consistent with a diagnosis of HAE types I/II. The decision on when to use long-term prophylaxis cannot be made on rigid criteria but should reflect the needs of the individual patient. First-line medications for HAE I/II include intravenous C1-INH, Haegarda® (C1-INH [human] subcutaneous injection), or Takhzyro® (lanadelumab-flyo subcutaneous injection).

According to World Allergy Organization guidelines (2025), it is recommended to evaluate for long-term prophylaxis at every visit, with a shared decision-making approach.[3] Access to on-demand therapy is recommended even while receiving long-term prophylaxis. The following therapies are supported as first-line options for long-term prophylaxis: subcutaneous plasma-derived C1-INH(Haegarda), Takhzyro , Andembry, Orladeyo® (berotralstat capsules) and Dawnzera™ (donidalorsen subcutaneous injection). The quality of evidence was "low", meaning further research is likely to have a significant impact and may change the recommendations. However, the agreement level among the experts was at 94% for this recommendation. Plasma-derived C1-INH, attenuated androgens at the lowest effective dose (preferably not exceeding 200 mg per day), or antifibrinolytics are second-line options for long-term prophylaxis in patients for whom the first-line therapies are not available, not feasible, or not tolerated. The guidelines note that intravenous plasma-derived C1-INH therapies are supported by scientific evidence for its efficacy, but it has disadvantages such as need for venous access, high cost, and frequent administrations due to its short half-life. The quality of evidence is noted as "low" with a 94% agreement level for this recommendation. It is unclear if these recommendations apply to HAE with normal C1-INH. The guidelines note in the text (not as a recommendation statement) that patients with HAE normal C1 INH have been successfully treated with Takhzyro, Andembry, intravenous C1-INH, or Orladeyo. No data on case reports are included. It is also noted that genetic testing is essential to determine with medication would be most appropriate; in patients with negative genetic testing, Takhzyro failed to demonstrate any significant benefit.

POLICY STATEMENT

Prior Authorization is recommended for medical benefit coverage of Andembry. Approval is recommended for those who meet the Criteria and Dosing for the listed indication. Extended approvals are allowed if the patient continues to meet the Criteria and Dosing. Requests for doses outside of the established dosing documented in this policy will be considered on a case-by-case basis by a clinician (i.e., Medical Director or Pharmacist). All approvals are provided for the duration noted below. Because of the specialized skills

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required for evaluation and diagnosis of patients treated with Andembry as well as the monitoring required for adverse events and long-term efficacy, approval requires Andembry to be prescribed by or in consultation with a physician who specializes in the condition being treated. A patient who has previously met initial therapy criteria for Andembry for the requested indication under the Coverage Review Department and is currently receiving the requested therapy is only required to meet the continuation therapy criteria (i.e., currently receiving Andembry). If past criteria have not been met under the Coverage Review Department and the patient is currently receiving Andembry, initial therapy criteria must be met.
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. All documentation must include patient-specific identifying information.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

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

FDA-Approved Indication

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1. **Hereditary Angioedema (HAE) Due to C1 Inhibitor (C1-INH) Deficiency – Prophylaxis.** Approve Andembry for 1 year if the patient meets ONE of the following (A or B):
   - **A)** Initial therapy. Approve if the patient meets ALL of the following (i, ii, and iii):
     - **i.** Patient is ≥ 12 years of age; AND
     - **ii.** Patient has HAE type I or type II as confirmed by the following diagnostic criteria (a and b):
       Note: A diagnosis of HAE with normal C1-INH (also known as HAE type III) does NOT satisfy this requirement.
       - **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
     - **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; OR
   - **B)** Patient is Currently Receiving Andembry. Approve if the patient meets ALL of the following (i, ii, and iii):
     Note: If the patient is currently receiving the requested therapy, but has not previously received approval of Andembry for this indication through the Coverage Review Department, review under criteria for Initial Therapy.
     - **i.** Patient has a diagnosis of HAE type I or type II **[documentation required]**; AND
       Note: A diagnosis of HAE with normal C1-INH (also known as HAE type III) does NOT satisfy this requirement.
     - **ii.** According to the prescriber, the patient has had a favorable clinical response since initiating Andembry prophylactic therapy compared with baseline (i.e., prior to initiating prophylactic therapy); AND
       Note: Examples of a 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.

   Dosing. Approve ONE of the following dosing regimens (A or B):

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A) Loading dose of 400 mg as a subcutaneous one-time injection; OR
B) Maintenance dose of 200 mg as a subcutaneous injection not more frequently than once every month.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Andembry is not recommended in the following situations:

1. **Concomitant Use with Other Hereditary Angioedema (HAE) Prophylactic Therapies.** Andembry 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® (C1 esterase inhibitor [human] intravenous infusion), for on-demand treatment of acute HAE attacks, and for short-term (procedural) prophylaxis.
   Note: Examples of other HAE prophylactic therapies include Cinryze (C1 esterase inhibitor [human] intravenous infusion), Haegarda (C1 esterase inhibitor [human] subcutaneous injection), Orladeyo (berotralstat capsules), and Takhzyro (lanadelumab-flyo subcutaneous injection).

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. Andembry® subcutaneous injection [prescribing information]. King of Prussia, PA: CSL Behring; June 2025.
2. Busse PJ, Christiansen SC, Riedl MA, et al. US HAEA Medical Advisory Board 2020 guidelines for the management of hereditary angioedema. *J Allergy Clin Immunol Pract*. 2021;9(1):132-150.e3.
3. Vazquez DO, Giavina-Bianchi P, Josviack D, et al. The 2025 WAO guidelines for the classification, diagnosis, and treatment of hereditary angioedema, with consideration of worldwide disparities [Article in Press]. *World Allergy Organ J*. Published online 2026. Doi:10.1016/j.waojou.2026.101335.

HISTORY

Type of Revision	Summary of Changes	Review Date
New Policy	--	06/18/2025
Selected Revision	**Hereditary Angioedema (HAE) Due to C1 Inhibitor (C1-INH) Deficiency – Prophylaxis:** In reference to low levels of functional C1-INH protein levels, changed from "(≤ 50% of normal)" to "(< 50% of normal)".	10/01/2025
Annual Revision	No criteria changes.	05/13/2026

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