Drug Coverage Policy

Effective Date.....01/15/2026
Coverage Policy Number.....IP0756
Policy Title.....Ekterly

Hereditary Angioedema - Ekterly

- Ekterly® (sebetralstat tablets - KalVista Pharmaceuticals)

INSTRUCTIONS FOR USE
The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Each coverage request should be reviewed on its own merits. Medical directors are expected to exercise clinical judgment where appropriate and have discretion in making individual coverage determinations. Where coverage for care or services does not depend on specific circumstances, reimbursement will only be provided if a requested service(s) is submitted in accordance with the relevant criteria outlined in the applicable Coverage Policy, including covered diagnosis and/or procedure code(s). Reimbursement is not allowed for services when billed for conditions or diagnoses that are not covered under this Coverage Policy (see "Coding Information" below). When billing, providers must use the most appropriate codes as of the effective date of the submission. Claims submitted for services that are not accompanied by covered code(s) under the applicable Coverage Policy will be denied as not covered. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Overview

Ekterly, a plasma kallikrein inhibitor, is indicated for the **treatment of acute 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 goal of acute therapy is to minimize morbidity and prevent mortality from an ongoing HAE attack. Patients must have ready access to effective on-demand medication to administer at the onset of an HAE attack. All HAE attacks are eligible for treatment, irrespective of the location of swelling or severity of the attack. First-line treatments include plasma-derived C1-INH, Ruconest® (C1-INH [recombinant] intravenous [IV] infusion), Kalbitor® (ecallantide subcutaneous injection), and icatibant.

In guidelines from the World Allergy Organization/European Academy of Allergy and Clinical Immunology (2021), it is recommended that all attacks be treated with either IV C1-INH, Kalbitor, or icatibant (evidence level A for all).[3] Regarding IV C1-INH, it is noted that Berinert® (C1 esterase inhibitor [human] IV infusion) and Cinryze® (C1 esterase inhibitor [human] IV infusion) are both plasma-derived products available for this use, although indications vary globally. It is essential that patients have on-demand medication to treat all attacks; thus, the guidelines recommend that patients have and carry medication for treatment of at least two attacks.

An international consensus paper was published on the diagnosis, pathophysiology, and treatment of HAE-nl-C1INH.[4] The paper notes there is a paucity of high-level evidence in HAE-nC1INH and that all recommendations are based on expert opinion. Mutations in six different genes have been linked to HAE-nC1INH; however, the paper also specifies that many patients still lack an identified pathogenic variant for HAE-nC1INH.

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Policy Statement
Prior Authorization is required for benefit coverage of Ekterly. All approvals are provided for the duration noted below. Because of the specialized skills required for evaluation and diagnosis of patients treated with Ekterly, approval requires Ekterly 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 Ekterly 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., patient who has treated previous HAE attacks with Ekterly). If past criteria have not been met under the Coverage Review Department and the patient has treated previous HAE attacks with Ekterly, initial therapy criteria must be met.

Documentation: Documentation is required for use of Ekterly as noted in the criteria as **[documentation required].** Documentation may include, but is not limited to, chart notes, prescription claims records, prescription receipts, and/or other information.

Ekterly is considered medically necessary when the following are met:

FDA-Approved Indication

1. **Hereditary Angioedema (HAE) Due to C1 Inhibitor (C1-INH) Deficiency – Treatment of Acute Attacks.** Approve 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, iii, and iv):
      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.
      iv. Preferred product criteria is met for the product(s) as listed in the below table(s)
   B) Patient who has treated previous HAE attacks with Ekterly. 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 Ekterly 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 with Ekterly treatment; AND
      Note: Examples of a favorable clinical response include decrease in the duration of HAE attacks, quick onset of symptom relief, complete resolution of symptoms, or decrease in HAE acute attack frequency or severity.
      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.

Employer Plans

Product	Criteria
Ekterly (sebetralstat tablets)	Patient meets one of the following (1, 2, or 3): 1. Patient is ≥ 12 years of age and < 18 years of age. 2. Patient has previously treated an acute HAE attack with Ekterly. 3. Patient has tried generic icatibant Note: A previous trial of any icatibant product would count toward Criteria 3.

Individual and Family Plans:

Product	Criteria
Ekterly (sebetralstat tablets)	Patient meets one of the following (1, 2, or 3): 1. Patient is ≥ 12 years of age and < 18 years of age. 2. Patient has previously treated an acute HAE attack with Ekterly. 3. Patient has tried generic icatibant or Sajazir Note: A previous trial of any icatibant product would count toward Criteria 3.

Conditions Not Covered

Ekterly for any other use is considered not medically necessary, including the following (this list may not be all inclusive; criteria will be updated as new published data are available):

1. **Hereditary Angioedema (HAE) Prophylaxis.** Data are not available and Ekterly is not indicated for prophylaxis of HAE attacks.

References

1. Ekterly® tablets [prescribing information]. Cambridge, MA: KalVista Pharmaceuticals; July 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. Maurer M, Magerl M, Betschel S, et al. The international WAO/EAACI guideline for the management of hereditary angioedema: the 2021 revision and update. *Allergy*. 2022;77(7):1961-1990.
4. Zuraw BL, Bork K, Bouillet L, et al. Hereditary angioedema with normal C1 inhibitor: an updated international consensus paper on diagnosis, pathophysiology, and treatment. *Clin Rev Allergy Immunol.* 2025;68:24.

Revision Details

Type of Revision	Summary of Changes	Date
New	New policy.	01/15/2026

The policy effective date is in force until updated or retired.