

## **Clinical Policy: Ecallantide (Kalbitor)**

Reference Number: CP.PHAR.177

Effective Date: 03.01.16

Last Review Date: 02.18

Line of Business: Commercial, Medicaid

[Coding Implications](#)

[Revision Log](#)

See [Important Reminder](#) at the end of this policy for important regulatory and legal information.

### **Description**

Ecallantide (Kalbitor<sup>®</sup>) is a plasma kallikrein inhibitor.

### **FDA Approved Indication(s)**

Kalbitor is indicated for treatment of acute attacks of hereditary angioedema (HAE) in patients 12 years of age and older.

### **Policy/Criteria**

*Provider must submit documentation (including such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.*

It is the policy of health plans affiliated with Centene Corporation<sup>®</sup> that Kalbitor is **medically necessary** when the following criteria are met:

## **I. Initial Approval Criteria**

### **A. Hereditary Angioedema (must meet all):**

1. Diagnosis of HAE confirmed by one of the following (a or b):
  - a. Low C4 level and low C1-INH antigenic or functional level (*see Appendix C*);
  - b. Normal C4 level and normal C1-INH levels, and all of the following (i and ii):
    - i. History of recurrent angioedema;
    - ii. Family history of angioedema;
2. Prescribed by or in consultation with a hematologist, allergist, or immunologist;
3. Age  $\geq$  12 years;
4. Prescribed for treatment of acute HAE attacks;
5. Dose does not exceed 30 mg per dose (1 carton [3 vials] per dose) with up to 2 doses administered in a 24 hour period.

#### **Approval duration:**

**Medicaid – 12 months**

**Commercial – Length of benefit**

### **B. Other diagnoses/indications**

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial and CP.PMN.53 for Medicaid.

## **II. Continued Therapy**

### **A. Hereditary Angioedema (must meet all):**

1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
2. Member is responding positively to therapy;
3. If request is for a dose increase, new dose does not exceed 30 mg per dose (1 carton [3 vials] per dose) with up to 2 doses administered in a 24 hour period.

**Approval duration:**

**Medicaid – 12 months**

**Commercial – Length of benefit**

**B. Other diagnoses/indications (must meet 1 or 2):**

1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.

**Approval duration: Duration of request or 6 months (whichever is less);** or

2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial and CP.PMN.53 for Medicaid.

**III. Diagnoses/Indications for which coverage is NOT authorized:**

- A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.CPA.09 for commercial and CP.PMN.53 for Medicaid or evidence of coverage documents.

**IV. Appendices/General Information**

*Appendix A: Abbreviation/Acronym Key*

CI-INH: C1 esterase inhibitor

FDA: Food and Drug Administration

HAE: hereditary angioedema

*Appendix B: Therapeutic Alternatives*

Not applicable

*Appendix C: General Information*

- Diagnosis of HAE:
  - There are two classifications of HAE: HAE with C1-INH deficiency (further broken down into Type 1 and Type II) and HAE of unknown origin (also known as Type III).
  - In both Type 1 (~85% of cases) and Type II (~15% of cases), C4 levels are low. C1-INH antigenic levels are low in Type I while C1-INH functional levels are low in Type II. Diagnosis of Type I and II can be confirmed with laboratory tests. Reference ranges for C4 and C1-INH levels can vary across laboratories (see below for examples); low values confirming diagnosis are those which are below the lower end of normal.

Laboratory Test & Reference Range	Mayo Clinic	Quest Diagnostics	LabCorp
C4	14-40 mg/dL	16-47 mg/dL	9-36 mg/dL

C1-INH, antigenic	19-37 mg/dL	21-39 mg/dL	21-39 mg/dL
C1-INH, functional	Normal: > 67% Equivocal: 41-67% Abnormal: < 41%	Normal: ≥ 68% Equivocal: 41-67% Abnormal: ≤ 40%	Normal: > 67% Equivocal: 41-67% Abnormal: < 41%

- Type III, on the other hand, presents with normal C4 and C1-INH levels. Some patients have an associated mutation in the FXII gene, while others have no identified genetic indicators. Type III is very rare (number of cases unknown), and there are no laboratory tests to confirm the diagnosis. Instead, the diagnosis is clinical and supported by recurrent episodes of angioedema with a strong family history of angioedema.

**V. Dosage and Administration**

Indication	Dosing Regimen	Maximum Dose
Acute attacks of HAE	30 mg (3 mL) administered SC in three 10 mg (1 mL) injections; if attack persists, an additional dose of 30 mg may be administered within a 24 hour period	30 mg/dose; 2 doses in 24 hours

**VI. Product Availability**

Vial with solution for injection: 10 mg/mL

**VII. References**

1. Kalbitor Prescribing Information. Burlington, MA: Dyax Corporation; March 2015. Available at: [www.kalbitor.com](http://www.kalbitor.com). Accessed November 16, 2017.
2. Cicardi M, Bork K, Caballero T, et al. Evidence-based recommendations for the therapeutic management of angioedema owing to hereditary C1 inhibitor deficiency: consensus report of an International Working Group. *Allergy*. 2012; 67(2): 147-157.
3. Cicardi M, Aberer W, Banerji A, et al. Classification, diagnosis, and approach to treatment for angioedema: consensus report from the Hereditary Angioedema International Working Group. *Allergy*. 2014; 69(5): 602-616.
4. Craig T, Pursun E, Bork K, et al. WAO guideline for the management of hereditary angioedema. *WAO Journal*. 2012; 5: 182-199.

**Coding Implications**

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J1290	Injection, ecallantide, 1 mg

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Medicaid: Policy converted to new template and split from CP.PHAR.46.HAE Treatment. Criteria: added max dose criteria per PI. Removed administration setting from criteria, as it is included in the Safety Information.	02.16	03.16
Medicaid: Added criteria to confirm diagnosis. Removed age requirement. Increased approval duration to 12 months, and incorporated recommended dosing from PI. Removed warning against hypersensitivity. Added criteria for continued approval.	03.17	03.17
1Q18 annual review: - Policies combined for Medicaid and commercial business - No significant changes from previously approved corporate policy - Medicaid: added specialist requirement, removed “Other types of angioedema have been ruled out” from part of diagnosis due to its subjective nature, while specialist has been added - Added age limit - References reviewed and updated.	11.15.17	02.18

**Important Reminder**

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. “Health Plan” means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan’s affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

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**Note:**

**For Medicaid members**, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

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