Clinical Policy: Ecallantide (Kalbitor)

Reference Number: PA.CP.PHAR.177
Effective Date: 01/18
Last Review Date: 07/18

Coding Implications
Revision Log

Description
The intent of the criteria is to ensure that patients follow selection elements established by Pennsylvania Health and Wellness® clinical policy for ecallantide (Kalbitor®).

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
It is the policy of Pennsylvania Health and Wellness® that Kalbitor is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Hereditary Angioedema (HAE) (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 B);
   b. Normal C4 level and normal C1-INH levels, and all of the following (i - 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 ≥ 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: 12 months

B. Other diagnoses/indications: Refer to PA.CP.PMN.53

II. Continued Approval

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

1. Currently receiving medication via Pennsylvania Health and Wellness benefit or member has previously met initial approval criteria, or the Continuity of Care policy (PA.LTSS. PHAR.01) applies;
2. Documentation of positive response to therapy;
3. Prescribed 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.
   a. Quantities requested above limits will be reviewed for necessity. Exceptions will be allowed for patients maximizing prophylactic therapies and medical record documentation of acute attacks requiring more than four doses per month.

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2):
1. Currently receiving medication via Pennsylvania Health and Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.LTSS. PHAR.01) applies; or
2. Refer to PA.CP.PMN.53

Background

Description/Mechanism of Action:

Kalbitor (ecallantide) is a potent, selective, reversible inhibitor of plasma kallikrein. Kalbitor binds to plasma kallikrein and blocks its binding site, inhibiting the conversion of high molecular weight kininogen to bradykinin. By directly inhibiting plasma kallikrein, Kalbitor reduces the conversion of high molecular weight kininogen to bradykinin and thereby treats symptoms of the disease during acute episodic attacks of HAE.

Formulations:
Kalbitor is supplied as three 10 mg/mL single-use vials packaged in a carton. Each vial contains 10 mg of ecallantide with slight overfill.

Appendices

Appendix A: Abbreviation Key

ACE-I: angiotensin-converting enzyme inhibitor
ARB: angiotensin receptor blocker
CI-INH: C1 esterase inhibitor
HAE: hereditary angioedema

Appendix B: 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.

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	Approval Date
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.	02.18	

References
1. Kalbitor Prescribing Information. Burlington, MA: Dyax Corporation; March 2015. Available at: 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.
5.