Medical Policy:

Kalbitor® (ecallantide)

POLICY NUMBER	LAST REVIEW	ORIGIN DATE
MG.MM.PH.35	March 28, 2025	

Definition

Hereditary angioedema is an autosomal dominant condition marked by unpredictable and recurrent potentially fatal angioedema attacks; treatment options include injectable drugs for prophylaxis or for acute attacks.

Length of Authorization

Coverage will be provided for 6 months

Dosing Limits [Medical Benefit]

Max Units (per dose and over time):

- 30 billable units per dose up to 2 times in a 24-hour period once per week (240 billable units per 28 days)

Guideline

Kalbitor (ecallantide) is considered medically necessary for the **treatment of acute attacks of hereditary angioedema** when the following criteria are met:

(*Provider must submit documentation (which may include office chart notes and lab results) supporting that member*

has met all approval criteria):

A. Patient is 12 years of age or older; **AND**
B. Kalbitor is prescribed by, or in consultation with, a specialist in: allergy, immunology, hematology, pulmonology, or medical genetics; **AND**
C. Due to the risk of anaphylaxis, Kalbitor should only be administered by a healthcare professional with appropriate medical support to manage anaphylaxis and hereditary angioedema. Healthcare professionals should be aware of the similarity of symptoms between hypersensitivity reactions and hereditary angioedema and patients should be monitored closely; **AND**
D. Confirmation the patient is avoiding medications known to cause angioedema (e.g., ACE inhibitors, oral contraceptives, hormone replacement therapy, Dipeptidyl peptidase IV (DPP-IV) inhibitors, Neprilysin inhibitors); **AND**
E. Member has a history of moderate to severe cutaneous or abdominal attacks **OR** mild to severe airway swelling attacks of HAE (i.e. debilitating cutaneous/gastrointestinal symptoms or laryngeal/pharyngeal/tongue swelling); **AND**
F. Dose does not exceed 30 mg per dose (in three 10 mg 1 ml injections), with up to 2 doses administered in a 24-hour period; **AND**
G. Member has one of the following clinical presentations (table below) consistent with HAE subtype:

HAE I (C1-Inhibitor deficiency)
▪ Low C1 inhibitor- (C1-INH) antigenic level (C1-INH antigenic level below the lower limit of normal as defined by the laboratory performing the test); **AND** ▪ Low C4 level (C4 below the lower limit of normal as defined by the laboratory performing the test); **AND** ▪ Low C1-INH functional level (C1-INH functional level below the lower limit of normal as defined by the laboratory performing the test); **AND** o Member has a family history of HAE; **OR** o Normal C1q level
HAE II (C1-inhibitor dysfunction)
▪ Normal to elevated C1-INH antigenic level; **AND** ▪ Low C4 level (C4 below the lower limit of normal as defined by the laboratory performing the test); **AND** ▪ Low C1-INH functional level (C1-INH functional level below the lower limit of normal as defined by the laboratory performing the test)
HAE with normal C1NH (formerly known as HAE III)
▪ Normal C1-INH antigenic level; **AND** ▪ Normal C4 level; **AND** ▪ Normal C1-INH functional level; **AND** o Member has a known HAE-causing mutation (e.g., mutation of coagulation factor XII gene [F12 mutation], mutation in the angiopoietin-1 gene, mutation in the plasminogen gene); **OR** o Member has a family history of HAE

Coverage for Kalbitor (ecallantide) may be renewed when the following criteria are met:

1. Member continues to meet the criteria in the initial guideline; **AND**
2. Significant improvement in severity and duration of attacks have been achieved and sustained; **AND**
3. Absence of unacceptable toxicity from the drug (e.g., hypersensitivity reactions, thrombotic events, laryngeal attacks); **AND**
4. If request is for a dose increase, new dose does not exceed 30 mg per dose (in three 10 mg 1 ml injections), with up to 2 doses administered in a 24 hour period.

Limitations/Exclusions

1. Approval will be granted for 6 months and may be renewed
2. The cumulative amount of medication(s) the patient has on-hand, indicated for the acute treatment of HAE, will be taken into account when authorizing. The authorization will provide a sufficient quantity in order for the patient to have a cumulative amount of HAE medication on-hand in order to treat up to 4 acute attacks per 4 weeks for the duration of the authorization.
3. Use of Kalbitor (ecallantide) is considered experimental or investigational for all other uses.

Applicable Procedure Codes

Code	Description
J1290	Injection, ecallantide, 1 mg

Applicable NDCs

Code	Description
47783-0101-01	KALBITOR 10mg/mL Solution J1290 Injection, ecallantide, 1 mg

ICD-10 Diagnoses

Code	Description
D84.1	Defects in the complement system

Revision History

Company(ies)	DATE	REVISION
EmblemHealth & ConnectiCare	03/28/2025	Annual Review: Updated dosing limits. No criteria changes.
EmblemHealth & ConnectiCare	2/15/2024	Annual Review: Initial Criteria: Added Dipeptidyl peptidase IV (DPP-IV) inhibitors, Neprilysin inhibitors) as examples of medications to avoid.
EmblemHealth & ConnectiCare	6/22/2023	Annual Review: no criteria changes
EmblemHealth & ConnectiCare	08/08/2022	Transferred policy to new template
EmblemHealth & ConnectiCare	10/14/2019	Annual review

References

1. Caballero T, Farkas H, Bouillet L, et al.; C-1-INH Deficiency Working Group. International consensus and practical guidelines on the gynecologic and obstetric management of female patients with hereditary angioedema caused by C1 inhibitor deficiency. J Allergy Clin Immunol. 2012; 129(2):308-320.

2. Cicardi M, Bork K, Caballero T, et al.; HAWK (Hereditary Angioedema International Working Group). 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. Craig T, Aygören-Pürsün EA, Bork K, et al. World Allergy Organization (WAO) guideline for the management of hereditary angioedema. World Allergy Organ J. 2012; 5(12):182-199.
4. Lang DM, Aberer W, Bernstein JA, et al. International consensus on hereditary and acquired angioedema. Ann Allergy Asthma Immunol. 2012; 109(6):395-402.
5. U.S. Hereditary Angioedema Association (HAEA) Advisory Board. HAEA Consensus Document: An approach to diagnosis and treatment of HAE. 2013. http://www.haea.org/us-hereditary-angioedema-association-medical-advisory-board-2013-recommendations-management-hereditary-angioedema-due-c1-inhibitor-deficiency/ 2013.pdf. Accessed June 5, 2017.
6. https://www.shirecontent.com/PI/PDFs/Kalbitor_USA_ENG.pdf
7. Zuraw BL, Banerji A, Bernstein J, et al. U.S. Hereditary Angioedema Association (US HAE) Medical Advisory Board 2013 recommendations for the management of hereditary angioedema due to C1 inhibitor deficiency. J Allergy Clin Immunol. 2013a; 1(5):458-467.
8. Specialty-matched clinical peer review.
9. Kalbitor [package insert]. Burlington MA; Dyax Corporation; Revised March 2015. Accessed October 2019.