Geisinger

POLICIES AND PROCEDURE MANUAL

Policy: MBP 86.0

Section: Medical Benefit Pharmaceutical Policy

Subject: Kalbitor (ecallantide)

I. Policy:
Kalbitor (ecallantide)

II. Purpose/Objective:
To provide a policy of coverage regarding Kalbitor (ecallantide)

III. Responsibility:
A. Medical Directors
B. Medical Management
C. Pharmacy Department

IV. Required Definitions
1. Attachment – a supporting document that is developed and maintained by the policy writer or department requiring/authoring the policy.
2. Exhibit – a supporting document developed and maintained in a department other than
3. the department requiring/authoring the policy.
4. Devised – the date the policy was implemented.
5. Revised – the date of every revision to the policy, including typographical and grammatical changes.
6. Reviewed – the date documenting the annual review if the policy has no revisions necessary.

V. Additional Definitions
Medical Necessity or Medically Necessary means Covered Services rendered by a Health Care Provider that the Plan determines are:

a. appropriate for the symptoms and diagnosis or treatment of the Member's condition, illness, disease or injury;
b. provided for the diagnosis and the direct care and treatment of the Member's condition, illness disease or injury;
c. in accordance with current standards good medical treatment practiced by the general medical community;
d. not primarily for the convenience of the Member, or the Member's Health Care Provider; and
e. the most appropriate source or level of service that can safely be provided to the Member. When applied to hospitalization, this further means that the Member requires acute care as an inpatient due to the nature of the services rendered or the Member's condition, and the Member cannot receive safe or adequate care as an outpatient

Medicaid Business Segment
Medically Necessary — A service, item, procedure, or level of care compensable under the Medical Assistance program that is necessary for the proper treatment or management of an illness, injury, or disability is one that:

i. Will, or is reasonably expected to, prevent the onset of an illness, condition, injury or disability.
ii. Will, or is reasonably expected to, reduce or ameliorate the physical, mental or developmental effects of an illness, condition, injury or disability.
iii. Will assist the Member to achieve or maintain maximum functional capacity in performing daily activities, taking into account both the functional capacity of the Member and those functional capacities that are appropriate for Members of the same age.

DESCRIPTION:
Kalbitor (ecallantide) is a human plasma kallikrein inhibitor produced in Pichia pastoris yeast cells by recombinant DNA technology.

CRITERIA FOR USE: Requires Prior Authorization by Medical Director or Designee

GRANDFATHER PROVISION – Members already established on therapy are eligible for approval as long as there is medical record documentation that the safety and effectiveness of use for the prescribed indication is supported by Food and Drug Administration (FDA) approval or adequate medical and scientific evidence in the medical literature

Kalbitor (ecallantide) will be considered medically necessary for the commercial, exchange and CHIP lines of business for the treatment of acute attacks of hereditary angioedema in patients 12 years of age and older when the following criteria are met:

- Prescription is written by an allergist, immunologist, hematologist, or dermatologist **AND**
- Member is 12 years of age or older **AND**
- Medication is being used for the treatment of an acute attack of HAE **AND**
- Not used in combination with other approved treatments for acute HAE attacks **AND**
- Diagnosis of hereditary angioedema has been established and supported by physician provided documentation of:
    - Recurrent, self-limiting non-inflammatory subcutaneous angioedema without urticaria, lasting more than 12 hours **OR**
    - Laryngeal edema **OR**
    - Recurrent, self-remitting abdominal pain lasting more than 6 hours, without clear organic etiology

AND

- The presence of specific abnormalities in complement proteins, in the setting of a suggestive clinical history of episodic angioedema without urticaria; supported by
    - Medical record documentation of 2 or more sets of complement studies, separated by one month or more, showing consistent results of
        - Low C4 levels and
        - Less than 50% of the lower limit of normal C1-INH antigenic protein levels **OR**
        - Less than 50% of the lower limit of normal C1-INH function levels

AND

- Physician provided documentation of failure on, intolerance to, or contraindication to Berinert; **AND**
- Physician provided documentation of concurrent or failure on, intolerance to, or contraindication to prophylactic therapy (danazol).*

*Only applies to patients with more than one severe episode of angioedema per month, or those with a history of laryngeal attacks

QUANTITY LIMIT: 2 doses initially. Additional doses approved at the discretion of the Medical Director.

AUTHORIZATION DURATION: Initial approval will be for 6 months or less if the reviewing provider feels it is medically appropriate. Subsequent approvals will be for an additional 6 months or less if the reviewing provider feels it is medically appropriate and will require medical record documentation of continued disease improvement or lack of disease progression. The medication will no longer be covered if patient experiences toxicity or worsening of disease.

Kalbitor (ecallantide) will be considered medically necessary for the Medicare line of business for the treatment of acute attacks of hereditary angioedema in patients 12 years of age and older when the following criteria are met:

- Prescription is written by an allergist, immunologist, hematologist, or dermatologist **AND**
- Member is 12 years of age or older **AND**
- Medication is being used for the treatment of an acute attack of HAE **AND**
- Not used in combination with other approved treatments for acute HAE attacks **AND**
- Diagnosis of hereditary angioedema has been established and supported by physician provided documentation of:
    - Recurrent, self-limiting non-inflammatory subcutaneous angioedema without urticaria, lasting more than 12 hours **OR**
    - Laryngeal edema **OR**
    - Recurrent, self-remitting abdominal pain lasting more than 6 hours, without clear organic etiology

AND

- The presence of specific abnormalities in complement proteins, in the setting of a suggestive clinical history of episodic angioedema without urticaria; supported by
    - Medical record documentation of 2 or more sets of complement studies, separated by one month or more, showing consistent results of
        - Low C4 levels and
        - Less than 50% of the lower limit of normal C1-INH antigenic protein levels **OR**
        - Less than 50% of the lower limit of normal C1-INH function levels

QUANTITY LIMIT: 2 doses initially. Additional doses approved at the discretion of the Medical Director.

AUTHORIZATION DURATION: Initial approval will be for 6 months or less if the reviewing provider feels it is medically appropriate. Subsequent approvals will be for an additional 6 months or less if the reviewing provider feels it is medically appropriate and will require medical record documentation of continued disease improvement or lack of disease progression. The medication will no longer be covered if patient experiences toxicity or worsening of disease.

Comparison of complement studies in angioedema disorders

Angiodema disorder	C4*	C1 inhibitor level	C1 inhibitor function	C1q	C3	Other tests (not routinely needed for diagnosis)
HAE I	Low	Low	Low (usually <50 percent of normal)	Normal	Normal	Genetic testing
HAE II	Low	Normal or elevated	Low (usually <50 percent of normal)	Normal	Normal	Genetic testing
HAE III	Normal	Normal	Normal	Normal	Normal	Mutations in gene for factor XII detected in some patients
AAE	Low	Normal or low	Low (usually <50 percent of normal)	Normal or low•	Normal or low	Anti-C1 inhibitor antibodies
Idiopathic angioedema	Normal	Normal	Normal	Normal	Normal	

LINE OF BUSINESS:
Eligibility and contract specific benefit limitations and/or exclusions will apply. Coverage statements found in the line of business specific benefit document will supersede this policy.

REFERENCES:

1. Kalbitor [prescribing information]. Lexington, MA: Takeda Pharmaceuticals USA Inc; November 2021.
2. Busse, PJ, Christiansen SC, Riedl MA, et al. US HAEA Medical Advisory Board 2020 Guidelines for the Management of Hereditary Angioedema. US Hereditary Angioedema Association. Journal of Allergy clinical immunology Practice; 2020; 9(1):132-150 [cited 2023 Dec 27]. Available from: https://www.haea.org/pages/p/treatment_guidelines

This policy will be revised as necessary and reviewed no less than annually.

Devised: 9/8/10

Revised: 12/12, 08/14 3/24/15 (criteria, QL) 5/15/15 (medically necessary), 3/21/19 (grandfather), 1/17/23 (LOB carve out), 12/31/23 (references added), 1/9/24 (Medicaid business segment)

Reviewed: 10/11; 12/13, 08/14, 3/16, 3/30/17, 3/29/18, 2/28/19, 2/1/20, 1/19/21, 1/18/22

MA UM Committee approval: 12/31/23