Ecallantide

NDC CODE(S) 47783-0101-XX KALBITOR 10MG/ML Solution (SHIRE US INC.)

DESCRIPTION

Hereditary angioedema (HAE) is a rare genetic disorder caused by mutations to C1-esterase-inhibitor (C1-INH). It is characterized by low levels of C1-INH activity and low levels of C4. One function of C1-INH is as a major endogenous inhibitor of plasma kallikrein, part of the kallikrein-kinin system. This system is a complex cascade involved in both the inflammatory and coagulation pathways. Within this, one critical aspect is the conversion of High Molecular Weight (HMW) kininogen into bradykinin by plasma kallikrein. In HAE, normal regulation of plasma kallikrein activity and the complement cascade is not present. During attacks, unregulated activity of plasma kallikrein results in excessive in excessive bradykinin generation and is likely responsible for the characteristic HAE symptoms of localized swelling, inflammation and pain.

Ecallantide is a reversible inhibitor of plasma kallikrein. It binds to plasma kallikrein, effectively blocking its binding site and therefore prevents the conversion of HMW kininogen into bradykinin. This treats the symptoms of the disease during acute episodic attacks of HAE

POLICY

- Ecallantide for the treatment of acute attacks of hereditary angioedema is considered ***medically necessary*** if the medical appropriateness criteria are met. **(See Medical Appropriateness below.)**
- Ecallantide for the treatment of other conditions/diseases is considered ***investigational.***

MEDICAL APPROPRIATENESS

INITIAL APPROVAL

- Ecallantide is considered **medically appropriate** if **ALL** of the following criteria are met:
  - Individual is 12 years of age or older
  - Confirmation of avoidance of the following possible triggers of HAE attacks:
    - Estrogen-containing oral contraceptive agents and hormone replacement therapy
    - Antihypertensive agents containing ACE inhibitors
    - Dipeptidyl peptidase IV (DPP-IV) inhibitors (e.g., sitagliptin)
    - Neprilysin inhibitors (e.g., sacubitril)
  - Individual has a history of **ANY ONE** of the following:
    - Moderate to severe cutaneous attacks (without concomitant hives)
    - Abdominal attacks
    - Mild to severe airway swelling attacks of HAE (i.e. debilitating cutaneous/gastrointestinal symptoms or laryngeal/pharyngeal/tongue swelling)
  - Individual has one of the following clinical presentations consistent with a HAE subtype, which must be confirmed by repeat blood testing (treatment for acute attack should not be delayed for confirmatory testing):
    - **HAE I (C1-Inhibitor deficiency)** if **ALL** of the following:
      - Low C1-inhibitor (C1-INH) antigenic level (C1-INH antigenic level below the lower limit of normal as defined by the performing lab)
      - Low C4 level (C4 level below the lower limit of normal as defined by the performing lab)
      - Low C1-INH functional level (C1-INH functional level below the lower limit of normal as defined by the performing lab) and **ANY ONE** of the following:

  - Individual has a positive family history of HAE
  - Acquired angioedema has been ruled out (i.e., onset of symptoms occur prior to 30 years old, normal C1q levels, individual does not have underlying disease such as lymphoma or benign monoclonal gammopathy [MGUS], etc.)
- **HAE II (C1-inhibitor dysfunction)** if **ALL** of the following:
  - Normal to elevated C1-INH antigenic level
  - Low C4 (C4 below the lower limit of normal as defined by the performing lab)
  - Low C1-INH functional level (C1-INH functional level below the lower limit of normal as defined by the performing lab)
- **HAE with normal C1-INH (formerly known as HAE III)** if **ALL** of the following:
  - Normal C1-INH antigenic level
  - Normal C4 level
  - Normal C1-INH functional level
  - Repeat blood testing during an attack has confirmed the individual does not have abnormal lab values indicative of HAE I or HAE II
  - Individual has **ANY ONE** of the following:
    - Individual has known HAE-causing mutation (i.e., mutation of coagulation factor XII gene [F12 mutation], mutation in the angiopoietin-1 gene, mutation in the plasminogen gene etc.)
    - Individual has a family history of HAE and documented evidence of lack of efficacy of chronic high-dose antihistamine therapy *(e.g. cetirizine standard dosing at up to four times daily or an alternative equivalent, given for at least one month or an interval long enough to expect three or more angioedema attacks)* AND corticosteroids with or without omalizumab

RENEWAL CRITERIA

- Ecallantide is considered **medically appropriate** for renewal if **ALL** of the following criteria are met:
  - Individual continues to meet initial approval criteria
  - Significant improvement in severity and duration of attacks has been achieved and sustained
  - Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include hypersensitivity reactions, etc.
  - 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(s) on-hand in order to treat up to 4 acute attacks per 4 weeks for the duration of the authorization (unless otherwise specified).

INDICATION(S)	DOSAGE & ADMINISTRATION
Acute Hereditary Angioedema (HAE) attack	30 mg injected subcutaneously by a health care professional in three 10 mg injections. An additional dose of 30 mg may be administered if attack persists Not to exceed a total of two 30 mg doses (60 mg) in 24 hours.

LENGTH OF AUTHORIZATION

Coverage will be provided for 12 weeks and is eligible for renewal (unless otherwise specified).

The cumulative amount of medication(s) the individual 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 individual 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 (unless otherwise specified).

Refer to **DOSAGE LIMITS** below

APPLICABLE TENNESSEE STATE MANDATE REQUIREMENTS

BlueCross BlueShield of Tennessee's Medical Policy complies with Tennessee Code Annotated Section 56-7-2352 regarding coverage of off-label indications of Food and Drug Administration (FDA) approved drugs when the off-label use is recognized in one of the statutorily recognized standard reference compendia or in the published peer-reviewed medical literature.

IMPORTANT REMINDER

We develop Medical Policies to provide guidance to Members and Providers. This Medical Policy relates only to the services or supplies described in it. The existence of a Medical Policy is not an authorization, certification, explanation of benefits or a contract for the service (or supply) that is referenced in the Medical Policy. For a determination of the benefits that a Member is entitled to receive under his or her health plan, the Member's health plan must be reviewed. If there is a conflict between the Medical Policy and a health plan, the express terms of the health plan will govern.

ADDITIONAL INFORMATION

For appropriate chemotherapy regimens, dosage information, contraindications, precautions, warnings, and monitoring information, please refer to one of the standard reference compendia (e.g., the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) published by the National Comprehensive Cancer Network®, Drugdex Evaluations of Micromedex Solutions at Truven Health, or The American Hospital Formulary Service Drug Information).

SOURCES

Betschel, S., Badiou, J., Binkley, K., Borici-Mazi, R., Hébert, J., Kanani, A., et al. (2019). The International/Canadian Hereditary Angioedema Guideline. Allergy, Asthma & Clinical Immunology. 2019. 15:72. Published online 2019 Nov 25. doi: 10.1186/s13223-019-0376-8.

Lexicomp Online. (2020, March). AHFS DI. *Ecallantide*. Retrieved November 25, 2020 from Lexicomp Online with AHFS.

Maurer, M., Magerl, M., Ansotegui, I., Ayg€oren-P€urs€un, E., Betschel, S., Bork, K., et al. (2018). The international WAO/EAACI guideline for the management of hereditary angioedema-The 2017 revision and update. *Allergy,* 73 (8), 1575–1596.

MICROMEDEX Healthcare Series. Drugdex Evaluations. (2020, July). *Ecallantide*. Retrieved November 25, 2020 from MICROMEDEX Healthcare Series.

U. S. Food and Drug Administration. (2014, September). Center for Drug Evaluation and Research. *Kalbitor® (ecallantide) injection, for subcutaneous use.* Retrieved November 25, 2020 fromhttp://www.accessdata.fda.gov/drugsatfda_docs/label/2014/125277s071lbl.pdf.

EFFECTIVE DATE 4/2/21

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