PRIOR AUTHORIZATION POLICY

POLICY: Hereditary Angioedema – Kalbitor Prior Authorization Policy
- Kalbitor® (ecallantide injection for subcutaneous use – Dyax)

REVIEW DATE: 08/26/2020

OVERVIEW

Kalbitor, a plasma kallikrein inhibitor, is indicated for the treatment of acute attacks of hereditary angioedema (HAE) in patients ≥ 12 years of age.[1] Potentially serious hypersensitivity reactions, including anaphylaxis, have occurred in patients treated with Kalbitor. Kalbitor should only be administered by a healthcare professional with appropriate medical support to manage anaphylaxis and HAE.

Disease Overview

HAE due to C1 esterase inhibitor (C1-INH) deficiency has two subtypes: HAE type I and HAE type II. HAE diagnosis can be confirmed by measuring functional C1-INH protein levels (usually < 50% of normal in patients with HAE), C4 levels, and C1-INH antigenic levels.[2,3] Patients with HAE type I have low C4 and C1-INH antigenic protein levels, along with low levels of functional C1-INH protein. Patients with HAE type II have low C4 and functional C1-INH protein level, with a normal or elevated C1-INH antigenic protein level. C1-INH replacement therapies are appropriate for both HAE type I and type II.

Patients with the third type of HAE called HAE with normal C1-INH (HAE nC1-INH), previously referred to as HAE type III, have normal C4 and C1-INH antigenic protein levels.[2] HAE nC1-INH is much less prevalent than HAE types I/II, and the exact cause of HAE nC1-INH has not been determined.[2,4] Pathogenic variants in the genes encoding for Factor XII (regulates bradykinin generation), angiopoietin-1 (involved in vascular permeability), and plasminogen have been associated with HAE nC1-INH; however, the majority of cases have unknown etiology. There are no randomized or controlled clinical trial data available with any therapy for use in HAE nC1-INH.[4-6]

Guidelines

Per the World Allergy Organization/European Academy of Allergy and Clinical Immunology guidelines (2017), all HAE type I/II attacks should be considered for acute treatment; treatment is mandatory for any attack potentially affecting the upper airway (HAE nC1-INH is not addressed within the scope of the guideline).[3] Attacks should be treated as early as possible. Self-administration at home facilitates earlier response. The guidelines recommend C1-INH products, Kalbitor, or icatibant injection (Firazyr®, generics) as first-line treatment options. Androgens and anti-fibrinolytics are not effective as acute treatment. Patients should carry acute treatment with them at all times and should have enough supply on hand for treatment of two attacks. Other guidelines from the US Hereditary Angioedema Association Medical Advisory Board (2013), a practice parameter update from a Joint Task Force (2013), and an international and Canadian guideline (2019) have similar recommendations for acute treatment of HAE type I/II attacks.[4,7,8]

POLICY STATEMENT

Prior authorization is recommended for prescription benefit coverage of Kalbitor. Because of the specialized skills required for the evaluation and diagnosis of patients treated with Kalbitor, approval requires Kalbitor to be prescribed by or in consultation with a physician who specializes in the condition being treated. All approvals are provided for the duration noted below.

Documentation: Documentation will be required where noted in the criteria as **[documentation required]**. Documentation may include, but is not limited to, chart notes, laboratory records, and prescription claims records.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Kalbitor is recommended in those who meet the following criteria:

FDA-Approved Indications

1. **Hereditary Angioedema (HAE) Due to C1 Inhibitor (C1-INH) Deficiency [Type I or Type II] – Treatment of Acute Attacks.** Approve Kalbitor for the duration noted if the patient meets one of the following criteria (A or B):
   - **A)** Initial therapy. Approve for 1 year if the patient meets both of the following criteria (i and ii):
     - **i.** Patient has HAE type I or type II as confirmed by the following diagnostic criteria (a and b):
       - **a)** Patient has low levels of functional C1-INH protein (< 50% of normal) at baseline, as defined by the laboratory reference values **[documentation required]**; AND
       - **b)** Patient has lower than normal serum C4 levels at baseline, as defined by the laboratory reference values **[documentation required]**; AND
     - **ii.** The medication is prescribed by, or in consultation with, an allergist/immunologist or a physician that specializes in the treatment of HAE or related disorders.
   - **B)** Patient who has treated previous acute HAE attacks with Kalbitor. Approve for 1 year if the patient meets all of the following criteria (i, ii, and iii):
     - **i.** Patient has a diagnosis of HAE type I or II **[documentation required]**; AND
     - **ii.** According to the prescriber, the patient has had a favorable clinical response with Kalbitor treatment; AND
       Note: Examples of favorable clinical response include decrease in the duration of HAE attacks, quick onset of symptom relief, complete resolution of symptoms, or decrease in HAE acute attack frequency or severity.
     - **iii.** The medication is prescribed by or in consultation with an allergist/immunologist or a physician that specializes in the treatment of HAE or related disorders.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Kalbitor is not recommended in the following situations:

1. **Hereditary Angioedema (HAE) Prophylaxis.** Data are not available and Kalbitor is not indicated for the prophylaxis of HAE attacks.

2. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

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4. Betschel S, Badiou J, Binkley K, et al. The International/Canadian Hereditary Angioedema Guideline [published correction appears in Allergy Asthma Clin Immunol. 2020 May 6;16:33]. *Allergy Asthma Clin Immunol*. 2019;15:72. Available at: https://aacijournal.biomedcentral.com/articles/10.1186/s13223-019-0376-8. Accessed on August 4, 2020.
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