UTILIZATION MANAGEMENT MEDICAL POLICY

POLICY: Hereditary Angioedema – Kalbitor Utilization Management Medical Policy
- Kalbitor® (ecallantide subcutaneous injection – Takeda)

REVIEW DATE: 09/21/2022

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.

Guidelines

According to US HAE Association Medical Advisory Board Guidelines (2020), when HAE is suspected based on clinical presentation, appropriate testing includes measurement of the serum C4 level, C1 esterase inhibitor (C1-INH) antigenic level, and C1-INH functional level.[2] Low C4 plus low C1-INH antigenic or functional level is consistent with a diagnosis of HAE types I/II. The goal of acute therapy is to minimize morbidity and prevent mortality from an ongoing HAE attack. Patients must have ready access to effective on-demand medication to administer at the onset of an HAE attack. All HAE attacks are eligible for treatment, irrespective of the location of swelling or severity of the attack. First-line treatments include plasma-derived C1-INH, Ruconest® (C1-INH [recombinant] intravenous infusion), Kalbitor, and icatibant.

In guidelines from the World Allergy Organization/European Academy of Allergy and Clinical Immunology (2021), it is recommended that all attacks be treated with either IV C1-INH, Kalbitor, or icatibant (evidence level A for all).[3] Regarding IV C1-INH, it is noted that Berinert® (C1 esterase inhibitor [human] IV infusion) and Cinryze® (C1 esterase inhibitor [human] IV infusion) are both plasma-derived products available for this use, although indications vary globally. It is essential that patients have on-demand medication to treat all attacks; thus, the guidelines recommend that patients have and carry medication for treatment of at least two attacks.

POLICY STATEMENT

Prior Authorization is recommended for medical benefit coverage of Kalbitor. Approval is recommended for those who meet the **Criteria** and **Dosing** for the listed indication. Extended approvals are allowed if the patient continues to meet the Criteria and Dosing. Requests for doses outside of the established dosing documented in this policy will be considered on a case-by-case basis by a clinician (i.e., Medical Director or Pharmacist). All approvals are provided for the duration noted below. Because of the specialized skills required for evaluation and diagnosis of patients treated with Kalbitor, as well as monitoring required for adverse events and long-term efficacy, approval requires the medication to be prescribed by or in consultation with a physician who specializes in the condition being treated.

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 Indication

1. **Hereditary Angioedema (HAE) Due to C1 Inhibitor (C1-INH) Deficiency [Type I or Type II] – Treatment of Acute Attacks**. Approve Kalbitor for 1 year if the patient meets one of the following criteria (A or B):
   - **A)** Initial therapy. Approve 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):
       Note: A diagnosis of HAE with normal C1-INH (also known as HAE type III) does NOT satisfy this requirement.
       - **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 who specializes in the treatment of HAE or related disorders.
   - **B)** Patient who has treated previous acute HAE attacks with Kalbitor. Approve 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
       Note: A diagnosis of HAE with normal C1-INH (also known as HAE type III) does NOT satisfy this requirement.
     - **ii.** According to the prescriber, the patient has had a favorable clinical response with Kalbitor treatment; AND
       Note: Examples of a 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 who specializes in the treatment of HAE or related disorders.

   Dosing. Approve up to a maximum dose of 30 mg per injection, administered subcutaneously no more frequently than twice daily.

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 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

1. Kalbitor® subcutaneous injection [prescribing information]. Lexington, MA: Takeda; December 2020.
2. Busse PJ, Christiansen SC, Riedl MA, et al. US HAEA Medical Advisory Board 2020 guidelines for the management of hereditary angioedema. *J Allergy Clin Immunol Pract*. 2021;9(1):132-150.e3.
3. Maurer M, Magerl M, Betschel S, et al. The international WAO/EAACI guideline for the management of hereditary angioedema: the 2021 revision and update. *Allergy*. 2022;77(7):1961-1990.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	No criteria changes.	08/25/2021
Selected Revision	**Hereditary Angioedema (HAE) Due to C1 Inhibitor (C1-INH) Deficiency [Type I or Type II] – Treatment of Acute Attacks:** A Note was added to the initial and continuation criteria that a diagnosis of HAE with normal C1-INH (also known as HAE type III) does not satisfy the requirement for a diagnosis of HAE type I or type II.	06/01/2022
Annual Revision	No criteria changes.	09/21/2022