

UTILIZATION MANAGEMENT MEDICAL POLICY

POLICY: Hereditary Angioedema – Kalbitor Utilization Management Medical Policy

- Kalbitor® (ecallantide subcutaneous injection – Takeda)

REVIEW DATE: 10/15/2025

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.¹ 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 [IV] 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. A patient who has previously met initial therapy criteria for Kalbitor for the requested indication under the Coverage Review Department and is currently receiving the requested therapy, is only required to meet the continuation criteria (i.e., patient who has treated previous acute HAE attacks with Kalbitor). If past criteria have not been met under

the Coverage Review Department and the patient has treated previous HAE attacks with Kalbitor, initial therapy criteria must be met.

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. All documentation must include patient-specific identifying information.

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 – Treatment of Acute Attacks.

Approve Kalbitor for 1 year if the patient meets ONE of the following (A or B):

A) Initial therapy. Approve if the patient meets BOTH of the following (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; OR

B) Patient who has treated previous acute HAE attacks with Kalbitor. Approve if the patient meets ALL of the following (i, ii, and iii):

Note: If the patient is currently receiving the requested therapy but has not previously received approval of Kalbitor for this indication through the Coverage Review Department, review under criteria for Initial Therapy.

i. Patient has a diagnosis of HAE type I or type 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.
- Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

- Kalbitor® subcutaneous injection [prescribing information]. Lexington, MA: Takeda; December 2023.
- 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.
- 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	It was added to the Policy Statement that a person who has previously met initial therapy criteria for Kalbitor for the requested indication under the Coverage Review Department and has treated previous HAE attacks with Kalbitor, is only required to meet the continuation of therapy criteria (i.e., patient has treated previous HAE attacks with Kalbitor). If past criteria have not been met under the Coverage Review Department and the patient has treated previous HAE attacks with Kalbitor, initial criteria must be met. In addition, the following changes were made: Hereditary Angioedema (HAE) Due to C1 Inhibitor (C1-INH) Deficiency – Treatment of Acute Attacks: Deleted [Type I or Type II] from indication heading. Under criteria for “Patient who has treated previous HAE attacks with Kalbitor”, added a Note that patient has to meet initial therapy criteria and approval through the Coverage Review Department if they had previously received initial therapy approval through another entity. Also added the word “type” before II while referring to diagnosis of HAE types.	09/20/2023
Annual Revision	No criteria changes.	10/09/2024
Annual Revision	No criteria changes.	10/15/2025