BlueCross BlueShield
Federal Employee Program
Federal Employee Program®
750 9th St NW
Washington, D.C. 20001
202.942.1000
Fax 202.942.1125

5.85.007

Section:	Prescription Drugs	**Effective Date:**	July 1, 2024
Subsection:	Hematological Agents	**Original Policy Date:**	December 7, 2011
Subject:	Kalbitor	**Page:**	1 of 5

Last Review Date: June 13, 2024

Kalbitor

Description

Kalbitor (ecallantide)

Background

Kalbitor (ecallantide) is a human plasma kallikrein inhibitor for the treatment of acute attacks in adult and adolescent patients with hereditary angioedema (HAE). Hereditary angioedema, which is caused by having insufficient amounts of a plasma protein called C1-esterase inhibitor. People with HAE can develop rapid swelling of the hands, feet, limbs, face, intestinal tract, or airway. These acute attacks of swelling can occur spontaneously, or can be triggered by stress, surgery or infection. Swelling of the airway is potentially fatal without immediate treatment. Kalbitor is intended to restore the level of functional C1-esterase inhibitor in a patient's plasma, thereby treating the acute attack of swelling (1).

Regulatory Status

FDA-approved indication: Kalbitor is a plasma kallikrein inhibitor indicated for treatment of acute attacks of hereditary angioedema (HAE) in patients 12 years of age and older (1).

Kalbitor includes a boxed warning of serious hypersensitivity reactions, including anaphylaxis. Anaphylaxis has occurred in 4% of treated patients. Kalbitor should only be administered by a healthcare professional with appropriate medical support to manage anaphylaxis and hereditary angioedema (1).

The safety and efficacy of Kalbitor in pediatric patients less than 12 years of age have not been established (1).

Related policies
Berinert, Cinryze, Haegarda, Icatibant, Orladeyo, Ruconest, Takhzyro

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Kalbitor may be considered **medically necessary** if the conditions indicated below are met.

Kalbitor may be considered **investigational** for all other indications.

Prior-Approval Requirements

Age 12 years of age and older

Diagnosis

Patient must have the following:

1. Hereditary Angioedema (HAE) with **ONE** of the following:
    a. Patient has a C1 inhibitor deficiency or dysfunction as confirmed by laboratory testing **AND ALL** of the following:
        i. C4 level below the lower limit of normal as defined by the laboratory performing the test
        ii. C1 inhibitor (C1-INH) antigenic level below the lower limit of normal as defined by the laboratory performing the test **OR** normal C1-INH antigenic level and a low C1-INH functional level (functional C1-INH less than 50% or C1-INH functional level below the lower limit of normal as defined by the laboratory performing the test)
    b. Patient has normal C1 inhibitor as confirmed by laboratory testing **AND ONE** of the following:
        i. F12, angiopoietin-1, plasminogen, or kininogen-1 (KNG1) gene mutation as confirmed by genetic testing
        ii. Documented family history of angioedema and the angioedema was refractory to a trial of high-dose antihistamine (e.g.,

cetirizine) for at least one month

AND ALL of the following:

1. Used for acute attacks of hereditary angioedema
2. **NOT** being used for the routine prevention of hereditary angioedema attacks
3. Will be administered by a healthcare professional with appropriate medical support to manage anaphylaxis and hereditary angioedema
4. **NO** dual therapy with another agent for treating acute attacks of hereditary angioedema (e.g., Berinert, Firazyr/Sajazir, Ruconest)

Prior – Approval *Renewal* Requirements

Age 12 years of age and older

Diagnosis

Patient must have the following:

Hereditary Angioedema (HAE)

AND ALL of the following:

1. Used for acute attacks of hereditary angioedema
2. **NOT** being used for the routine prevention of hereditary angioedema attacks
3. Patient has experienced a reduction in severity and/or duration of hereditary angioedema attacks
4. Will be administered by a healthcare professional with appropriate medical support to manage anaphylaxis and hereditary angioedema
5. **NO** dual therapy with another agent for treating acute attacks of hereditary angioedema (e.g., Berinert, Firazyr/Sajazir, Ruconest)

Policy Guidelines

Pre - PA Allowance

None

Prior - Approval Limits

Duration 12 months

Prior – Approval *Renewal* Limits

Same as above

Rationale

Summary

Kalbitor (ecallantide) is a plasma kallikrein inhibitor indicated for the treatment of acute attacks in adult and adolescent patients with hereditary angioedema (HAE). HAE symptoms include episodes of edema (swelling) in various body parts including the hands, feet, face, and airway. HAE is caused by mutations to C1-esterase-inhibitor (C1-INH). The safety and efficacy of Kalbitor in pediatric patients less than 12 years of age have not been established (1).

Prior authorization is required to ensure the safe, clinically appropriate, and cost-effective use of Kalbitor while maintaining optimal therapeutic outcomes.

References

1. Kalbitor [package insert]. Lexington, MA : Dyax Corp.; November 2021.

Policy History

Date	Action
December 2011	New policy
September 2012	Annual editorial and reference update
March 2013	Annual editorial and reference update Addition to criteria that Kalbitor must be administered by a healthcare professional with appropriate medical support to manage anaphylaxis and hereditary angioedema.
June 2014	Annual review Revision of age to 12
December 2014	Annual editorial review and reference update Addition of the no dual therapy with another agent for treating acute attacks of HAE
December 2015	Annual review and reference update
December 2016	Annual editorial review and reference update. Changed Policy Code from 5.10.07 to 5.85.07
September 2017	Annual review
December 2017	Annual review

September 2018	Annual review
November 2018	Annual review
September 2019	Annual review
September 2020	Annual review
March 2021	Annual editorial review
April 2021	Added initiation requirements including C1 inhibitor testing, C4 testing, C1-INH testing, gene mutation testing, or documented family history of refractory angioedema and continuation requirement for significant reduction in severity and/or duration of HAE attacks since starting therapy per FEP
June 2021	Annual review
October 2021	Added Sajazir to no dual therapy list
December 2021	Annual review
June 2022	Annual review
June 2023	Annual review and reference update. Changed policy number to 5.85.007
December 2023	Annual review
June 2024	Annual review

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on June 13, 2024 and is effective on July 1, 2024.