

Specialty Guideline Management

Berinert

Products Referenced by this Document

Drugs that are listed in the following table include both brand and generic and all dosage forms and strengths unless otherwise stated. Over-the-counter (OTC) products are not included unless otherwise stated.

Brand Name	Generic Name
Berinert	C1 esterase inhibitor [human]

Indications

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications¹

Berinert is indicated for the treatment of acute abdominal, facial, or laryngeal hereditary angioedema (HAE) attacks in adult and pediatric patients.

Compendial Uses^{5,7}

Short-term preprocedural prophylaxis for HAE attacks.

All other indications are considered experimental/investigational and not medically necessary.

Documentation

Submission of the following information is necessary to initiate the prior authorization review:

Reference number(s)
1602-A

- For initial authorization, the following should be documented:
 - C1 inhibitor functional and antigenic protein levels
 - F12, angiotensin-1, plasminogen, kininogen-1 (KNG1), heparan sulfate-glucosamine 3-O-sulfotransferase 6 (HS3ST6), or myoferlin (MYOF) gene mutation testing, if applicable
 - Chart notes confirming family history of angioedema and the angioedema was refractory to a trial of high-dose antihistamine therapy, if applicable
- For continuation of therapy for acute attacks, chart notes demonstrating a reduction in severity and/or duration of attacks.

Prescriber Specialties

This medication must be prescribed by or in consultation with a prescriber who specializes in the management of HAE.

Coverage Criteria

Hereditary Angioedema (HAE)¹⁻²⁰

Preprocedural Prophylaxis

Authorization of 30 days may be granted for short-term preprocedural prophylaxis (i.e., prior to surgical or major dental procedures) when both of the following criteria are met at the time of diagnosis:

- Member meets either of the following criteria:
 - Member has C1 inhibitor deficiency or dysfunction as confirmed by laboratory testing and meets one of the following criteria:
 - 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).
 - Member has normal C1 inhibitor as confirmed by laboratory testing and meets one of the following criteria:
 - Member has an F12, angiotensin-1, plasminogen, kininogen-1 (KNG1), heparan sulfate-glucosamine 3-O-sulfotransferase 6 (HS3ST6), or myoferlin (MYOF) gene mutation as confirmed by genetic testing, or
 - Member has a documented family history of angioedema and the angioedema was refractory to a trial of high-dose antihistamine therapy (i.e., cetirizine at 40 mg per day or the equivalent) for at least one month.

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- Other causes of angioedema have been ruled out (e.g., angiotensin-converting enzyme inhibitor [ACE-I] induced angioedema, angioedema related to an estrogen-containing drug, allergic angioedema).

Acute Attacks

Authorization of 12 months may be granted for treatment of acute HAE attacks when the requested medication will not be used in combination with any other medication used for the treatment of acute HAE attacks and both of the following criteria are met at the time of diagnosis:

- Member meets either of the following criteria:
 - Member has C1 inhibitor deficiency or dysfunction as confirmed by laboratory testing and meets one of the following criteria:
 - 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).
 - Member has normal C1 inhibitor as confirmed by laboratory testing and meets one of the following criteria:
 - Member has an F12, angiotensin-1, plasminogen, kininogen-1 (KNG1), heparan sulfate-glucosamine 3-O-sulfotransferase 6 (HS3ST6), or myoferlin (MYOF) gene mutation as confirmed by genetic testing, or
 - Member has a documented family history of angioedema and the angioedema was refractory to a trial of high-dose antihistamine therapy (i.e., cetirizine at 40 mg per day or the equivalent) for at least one month.
- Other causes of angioedema have been ruled out (angiotensin-converting enzyme inhibitor [ACE-I] induced angioedema, angioedema related to an estrogen-containing drug, allergic angioedema).

Continuation of Therapy

Hereditary Angioedema (HAE)

Preprocedural Prophylaxis

All members (including new members) requesting authorization for continued short-term preprocedural prophylaxis (i.e., prior to surgical or major dental procedures) must meet all initial authorization criteria.

Acute Attacks

Authorization of 12 months may be granted for continued treatment of acute HAE attacks when all of the following criteria are met:

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- Member meets all requirements in the coverage criteria section.
- Member has experienced a reduction in severity and/or duration of acute attacks.
- Prophylaxis should be considered based on the attack frequency, attack severity, comorbid conditions, and member's quality of life.

References

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14. Henao MP, Kraschnewski J, Kelbel T, Craig T. Diagnosis and screening of patients with hereditary angioedema in primary care. *Therapeutics and Clin Risk Management.* 2016;12:701-711.
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Reference number(s)
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17. Craig T, Busse P, Gower RG, et al. Long-term prophylaxis therapy in patients with hereditary angioedema with C1 inhibitor deficiency. *Ann Allergy Asthma Immunol.* 2018;121(6):673-679.
18. Sharma J, Jindal AK, Banday AZ, et al. Pathophysiology of Hereditary Angioedema (HAE) Beyond the SERPING1 Gene [published online ahead of print, 2021 Jan 14] [published correction appears in *Clin Rev Allergy Immunol.* 2021 Feb 17]. *Clin Rev Allergy Immunol.* 2021;10.1007/s12016-021-08835-8. Doi:10.1007/s12016-021-08835-8.
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