

SPECIALTY GUIDELINE MANAGEMENT

BERINERT (C1 esterase inhibitor [human])

POLICY

I. 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.

A. FDA-Approved Indication

Treatment of acute abdominal, facial, or laryngeal hereditary angioedema (HAE) attacks in adult and pediatric patient

B. Compendial Use

Short-term preprocedural prophylaxis for HAE attacks

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

II. DOCUMENTATION

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

- A. For initial authorization, the following should be documented:
1. C4 levels and C1 inhibitor functional and antigenic protein levels
 2. F12, angiopoietin-1, plasminogen, kininogen-1 (KNG1), heparan sulfate-glucosamine 3-O-sulfotransferase 6 (HS3ST6), or myoferlin (MYOF) gene mutation testing, if applicable
 3. Chart notes confirming family history of angioedema, if applicable
- B. For continuation of therapy, chart notes demonstrating a reduction in severity and/or duration of attacks

III. CRITERIA FOR INITIAL APPROVAL

Hereditary Angioedema (HAE)

A. **Preprocedural Prophylaxis**

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

1. Member has C1 inhibitor deficiency or dysfunction as confirmed by laboratory testing and meets both of the following criteria:
 - i. Member has a C4 level below the lower limit of normal as defined by the laboratory performing the test, and
 - ii. Member meets one of the following criteria:
 - a. C1 inhibitor (C1-INH) antigenic level below the lower limit of normal as defined by the laboratory performing the test, or
 - b. 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).

2. Member has normal C1 inhibitor as confirmed by laboratory testing and meets one of the following criteria:
 - i. Member has an F12, angiotensin-converting enzyme 2 (ACE2), plasminogen, kininogen-1 (KNG-1), heparan sulfate-glucosaminase 3-O-sulfotransferase 6 (HS3ST6), or myoferlin (MYOF) gene mutation as confirmed by genetic testing, or
 - ii. 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.

B. Acute Attacks

Authorization of 6 months may be granted for treatment of acute hereditary angioedema attacks when the requested medication will not be used in combination with any other medication used for the treatment of acute HAE attacks and either of the following criteria is met:

1. Member has C1 inhibitor deficiency or dysfunction as confirmed by laboratory testing and meets both of the following criteria:
 - i. Member has a C4 level below the lower limit of normal as defined by the laboratory performing the test, and
 - ii. Member meets one of the following criteria:
 - a. C1 inhibitor (C1-INH) antigenic level below the lower limit of normal as defined by the laboratory performing the test, or
 - b. 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).
2. Member has normal C1 inhibitor as confirmed by laboratory testing and meets one of the following criteria:
 - i. Member has an F12, angiotensin-converting enzyme 2 (ACE2), plasminogen, kininogen-1 (KNG1), heparan sulfate-glucosaminase 3-O-sulfotransferase 6 (HS3ST6), or myoferlin (MYOF) gene mutation as confirmed by genetic testing, or
 - ii. 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.

IV. CONTINUATION OF THERAPY

Hereditary Angioedema

A. 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.

B. Acute Attacks

Authorization of 6 months may be granted for continued treatment of acute hereditary angioedema attacks when all of the following criteria are met:

1. Member meets the criteria for initial approval.
2. Member has experienced a reduction in severity and/or duration of attacks when the requested medication is used to treat an acute attack.
3. Prophylaxis should be considered based on the attack frequency, attack severity, comorbid conditions, and member's quality of life.

V. REFERENCES

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