



Beriner[®] (C1 Esterase Inhibitor, Human) (Intravenous)

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Medical Guideline Disclaimer

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I. Length of Authorization

Coverage will be provided for 12 weeks and is eligible for renewal.

The cumulative amount of medication(s) the patient has on-hand, indicated for the acute treatment of hereditary angioedema (HAE), will be taken into account when authorizing. The authorization will provide a sufficient quantity in order for the patient to have a cumulative amount of HAE medication(s) on-hand in order to treat up to 4 acute attacks per 4 weeks for the duration of the authorization.

II. Dosing Limits

A. Max Units (per dose and over time) [Medical Benefit]:

- 1100 billable units per 28 days

III. Initial Approval Criteria

Treatment of acute abdominal, facial, or laryngeal attacks of Hereditary Angioedema (HAE) †

- Must be prescribed by, or in consultation with, a specialist in: allergy, immunology, hematology, pulmonology, or medical genetics; **AND**

- Patient must be at least 6 years of age; **AND**
- Confirmation the patient is avoiding the following possible triggers for HAE attacks:
 - Estrogen-containing oral contraceptive agents AND hormone replacement therapy; **AND**
 - Antihypertensive agents containing ACE inhibitors; **AND**
- Patient has a history of moderate to severe cutaneous attacks without concomitant hives OR abdominal attacks OR mild to severe airway swelling attacks of HAE (i.e. debilitating cutaneous/gastrointestinal symptoms OR laryngeal/pharyngeal/tongue swelling); **AND**
- Patient has one of the following clinical presentations consistent with HAE subtype, which must be confirmed by repeat blood testing:

HAE I (C1-Inhibitor deficiency)

- Low C1 inhibitor (C1-INH) antigenic level (C1-INH antigenic level below the lower limit of normal as defined by the laboratory performing the test); **AND**
- Low C4 level (C4 below the lower limit of normal as defined by the laboratory performing the test); **AND**
- Low C1-INH functional level (C1-INH functional level below the lower limit of normal as defined by the laboratory performing the test); **AND**
 - Patient has a family history of HAE; **OR**
 - Onset of HAE symptoms occurred before age 30; **OR**
 - Normal C1q level

HAE II (C1-Inhibitor dysfunction)

- Normal to elevated C1-INH antigenic level; **AND**
- Low C4 level (C4 below the lower limit of normal as defined by the laboratory performing the test); **AND**
- Low C1-INH functional level (C1-INH functional level below the lower limit of normal as defined by the laboratory performing the test)

HAE with normal C1INH (also known as HAE III)

- Normal C1-INH antigenic level; **AND**
- Normal C4 level; **AND**
- Normal C1-INH functional level; **AND**
- Repeat blood testing during an attack has confirmed the patient does not have abnormal lab values indicative of HAE I or HAE II; **AND**
- Either of the following:
 - Patient has a known HAE-causing mutation (e.g., mutation of coagulation factor XII gene [F12 mutation], mutation in the angiotensin-1 gene, mutation in the plasminogen gene, etc.); **OR**

- Patient has a family history of HAE and documented evidence of lack of efficacy of chronic high-dose antihistamine therapy (*e.g. cetirizine standard dosing at up to four times daily or an alternative equivalent, given for at least one month or an interval long enough to expect three or more angioedema attacks*) AND corticosteroids

† FDA Approved Indication(s)

IV. Renewal Criteria

- Patient continues to meet the criteria above; **AND**
- Significant improvement in severity and duration of attacks have been achieved and sustained; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include the following: hypersensitivity reactions, serious thrombotic events, laryngeal HAE attacks, etc.; **AND**
- The cumulative amount of medication(s) the patient has on-hand, indicated for the acute treatment of HAE, will be taken into account when authorizing. The authorization will provide a sufficient quantity in order for the patient to have a cumulative amount of HAE medication(s) on-hand in order to treat up to 4 acute attacks per 4 weeks for the duration of the authorization.

V. Dosage/Administration

Indication	Dose
Hereditary Angioedema (HAE)	20 international units (IU) per kg body weight by intravenous injection upon recognition of an HAE attack.

Limitations/Exclusions

Beriner[®] (C1 Esterase Inhibitor, Human) is not considered medically necessary for indications other than those listed above due to insufficient evidence of therapeutic value.

Applicable Procedure Codes

J0597

Injection, C-1 esterase inhibitor (human), Beriner[®], 10 units

Applicable NDCs

63833-0825-xx

Beriner[®] 500 IU single-use vial

Applicable Diagnosis Codes

D84.1 Defects in the complement system

Revision History

VI. References

1. Beriner[®] [package insert]. Kankakee, IL; CSL Behring LLC; September 2017. Accessed December 2019.
2. Bygum A, Andersen KE, Mikkelsen CS. Self-administration of intravenous C1-inhibitor therapy for hereditary angioedema and associated quality of life benefits. *Eur J Dermatol*. Mar-Apr 2009;19(2):147-151.
3. Bowen T, Cicardi M, Farkas H, et al. 2010 International consensus algorithm for the diagnosis, therapy and management of hereditary angioedema. *Allergy Asthma Clin Immunol*. 2010;6(1):24.
4. Craig T, Aygören-Pürsün E, Bork K, et al. WAO Guideline for the Management of Hereditary Angioedema. *World Allergy Organ J*. 2012 Dec;5(12):182-99.
5. Gompels MM, Lock RJ, Abinun M, et al. C1 inhibitor deficiency: consensus document. *Clin Exp Immunol*. 2005;139(3):379.
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7. Betschel S, Badiou J, Binkley K, et al. Canadian hereditary angioedema guideline. *Asthma Clin Immunol*. 2014 Oct 24;10(1):50. doi: 10.1186/1710-1492-10-50.
8. Zuraw BL, Bernstein JA, Lang DM, et al. A focused parameter update: hereditary angioedema, acquired C1 inhibitor deficiency, and angiotensin-converting enzyme inhibitor-associated angioedema. *J Allergy Clin Immunol*. 2013 Jun;131(6):1491-3. doi: 10.1016/j.jaci.2013.03.034.
9. Zuraw BL, Banerji A, Bernstein JA, et al. US Hereditary Angioedema Association Medical Advisory Board 2013 recommendations for the management of hereditary angioedema due to C1 inhibitor deficiency. *J Allergy Clin Immunol Pract*. 2013 Sep-Oct;1(5):458-67.

10. Frank MM, Zuraw B, Banerji A, et al. Management of children with Hereditary Angioedema due to C1 Inhibitor deficiency. *Pediatrics*. 2016 Nov. 135(5)
11. Zuraw BL, Bork K, Binkley KE, et al. Hereditary angioedema with normal C1 inhibitor function: Consensus of an international expert panel. *Allergy Asthma Proc*. 2012;33 Suppl 1:145-156.
12. Maurer M, Mager M, Ansotegui I, et al. The international WAO/EAACI guideline for the management of hereditary angioedema-The 2017 revision and update. *Allergy*. 2018 Jan 10. doi: 10.1111/all.13384.