Mass General Brigham
Health Plan

Berinert (C1 esterase inhibitor [human])
Effective 07/01/2023

Plan	☐ MassHealth UPPL ☒Commercial/Exchange	**Program Type**	☒ Prior Authorization ☐ Quantity Limit ☐ Step Therapy
Benefit	☒ Pharmacy Benefit ☒ Medical Benefit		
Specialty Limitations	This medication has been designated specialty and must be filled at a contracted specialty pharmacy.		
Contact Information	**Medical and Specialty Medications** All Plans | Phone: 877-519-1908 | Fax: 855-540-3693		
	Non-Specialty Medications All Plans | Phone: 800-711-4555 | Fax: 844-403-1029		
Exceptions	N/A		

Overview

FDA-Approved Indication

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

Compendial Use

Short-term preprocedural prophylaxis for HAE attacks

Coverage Guidelines

Authorization may be granted for members new to the plan who are currently receiving treatment with the requested medication, excluding when the product is obtained as samples or via manufacturer's patient assistance programs.

OR

Authorization may be granted for treatment of Hereditary Angioedema (HAE) when all the following criteria are met:

Preprocedural Prophylaxis

1. Member is using requested medication for preprocedural prophylaxis (i.e., prior to surgical or major dental procedures)
2. Documentation that the member has C1 inhibitor deficiency or dysfunction as confirmed by laboratory testing and 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
    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).
3. Documentation that the member has normal C1 inhibitor as confirmed by laboratory testing and meets ONE of the following criteria:

a. Member has an F12, angiopoietin-1, plasminogen, kininogen-1 (KNG1), heparan sulfate-glucosamine 3-O-sulfotransferase 6 (HS3ST6), or myoferlin (MYOF) gene mutation as confirmed by genetic testing, or
b. 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.

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

Acute Attacks

1. The member is using requested medication for the treatment of acute HAE attacks
2. 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 at the time of diagnosis:
3. Documentation that the member has C1 inhibitor deficiency or dysfunction as confirmed by laboratory testing and 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).
4. Documentation that the member has normal C1 inhibitor as confirmed by laboratory testing and meets ONE of the following criteria:
    a. Member has an F12, angiopoietin-1, plasminogen, kininogen-1 (KNG1), heparan sulfate-glucosamine 3-O-sulfotransferase 6 (HS3ST6), or myoferlin (MYOF) gene mutation as confirmed by genetic testing, or
    b. 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.
5. Member has had inadequate response, adverse reaction or contraindication to generic Firazyr (icatibant)
6. This medication is prescribed by or in consultation with a prescriber who specializes in the management of HAE.

<u>Continuation of Therapy</u>

Reauthorization will be granted for HAE when provider submits the following:

1. **Preprocedural Prophylaxis**: requesting authorization for continued short-term preprocedural prophylaxis (i.e., prior to surgical or major dental procedures) must meet all initial authorization criteria.
2. **Acute Attacks**
    a. Member meets the criteria for initial approval.
    b. Physician attestation that the member has experienced a reduction in severity and/or duration of acute attacks.
    c. Prophylaxis should be considered based on the attack frequency, attack severity, comorbid conditions, and member's quality of life.

Limitations

1. Initial approvals will be granted for:
    a. Preprocedural prophylaxis: 30 days

b. Acute Attacks: 6 months

2. Reauthorizations will be granted for:
    a. Preprocedural prophylaxis: 30 days
    b. Acute Attacks: 6 months

References

1. Berinert [package insert]. Kankakee, IL: CSL Behring LLC; September 2021.
2. 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.
3. Cicardi M, Bork K, Caballero T, et al. Evidence-based recommendations for the therapeutic management of angioedema owing to hereditary C1 inhibitor deficiency: consensus report of an International Working Group. *Allergy.* 2012;67:147-157.
4. Kreuz W, Martinez-Saguer I, Aygoren-Pursun E. C1-inhibitor concentrate for individual replacement therapy in patients with severe hereditary angioedema refractory to danazol prophylaxis. *Transfusion.* 2009;49:1987-1995.
5. 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: In Practice.* 2021 Jan;9(1):132-150.e3.
6. 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(6):S145-S156.
7. Maurer M, Magerl M, Ansotegui I, et al. The international WAO/EAACI guideline for the management of hereditary angioedema – the 2021 revision and update. *Allergy.* 2022 Jan 10. doi: 10.1111/all. 15214. Online ahead of print.
8. Lang DM, Aberer W, Bernstein JA, et al. International consensus on hereditary and acquired angioedema. *Ann Allergy Asthma Immunol*. 2012;109:395-402.
9. Cicardi M, Aberer W, Banerji A, et al. Classification, diagnosis, and approach to treatment for angioedema: consensus report from the Hereditary Angioedema International Working Group. *Allergy*. 2014;69:602-616.
10. Bowen T. Hereditary angioedema: beyond international consensus – circa December 2010 – The Canadian Society of Allergy and Clinical Immunology Dr. David McCourtie Lecture. *Allergy Asthma Clin Immunol*. 2011;7(1):1.
11. Bernstein JA. Update on angioedema: Evaluation, diagnosis, and treatment. *Allergy and Asthma Proceedings.* 2011;32(6):408-412.
12. Longhurst H, Cicardi M. Hereditary angio-edema. *Lancet.* 2012;379:474-481.
13. Farkas H, Martinez-Saguer I, Bork K, et al. International consensus on the diagnosis and management of pediatric patients with hereditary angioedema with C1 inhibitor deficiency. *Allergy*. 2017;72(2):300-313.
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.
15. Bernstein J. Severity of hereditary angioedema, prevalence, and diagnostic considerations. *Am J Med.* 2018;24:292-298.
16. Bork K, Aygören-Pürsün E, Bas M, et al. Guideline: Hereditary angioedema due to C1 inhibitor deficiency. *Allergo J Int*. 2019;28:16–29.
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.

19. Kanani, A., Schellenberg, R. & Warrington, R. Urticaria and angioedema. *All Asth Clin Immun* 7, S9 (2011), Table 2.
20. Veronez CL, Csuka D, Sheik FR, et al. The expanding spectrum of mutations in hereditary angioedema. *J Allergy Clin Immunol Pract.* 2021;S2213-2198(21)00312-3.

Review History

05/10/2023 – Created for May P&T; switched from CVS SGM to custom. Effective 7/1/23