Policy Title:	Berinert (C1 esterase inhibitor [human]) (Intravenous)		
		Department:	PHA
Effective Date:	01/01/2020		
Review Date:	10/02/2019, 12/13/2019, 1/22/20, 5/06/2021, 2/10/2022, 3/16/2023, 12/14/2023, 01/04/2024		

Purpose: To support safe, effective, and appropriate use of Berinert (C1 esterase inhibitor [human]).

Scope: Medicaid, Commercial, Medicare-Medicaid Plan (MMP)

Policy Statement:

Berinert (C1 esterase inhibitor [human]) is covered under the Medical Benefit when used within the following guidelines. Use outside of these guidelines may result in non-payment unless approved under an exception process.

Procedure:

Coverage of Berinert (C1 esterase inhibitor [human]) will be reviewed prospectively via the prior authorization process based on criteria below.

Initial Criteria:

- Member is 6 years of age or older; AND
- Medication is prescribed by, or in consultation with allergist/immunologist or a physician who specializes in the treatment of HAE or related disorders; AND
- Berinert is being used for treatment of acute hereditary angioedema (HAE) attacks; AND
- Member has 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 documented diagnosis of HAE type I or type II and meets one of the following:
    - 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); OR
    - Member has normal C1 inhibitor as confirmed by laboratory testing and meets one of the following criteria:

- Member has an F12, angiopoietin-1, plasminogen, or 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 (e.g., cetirizine) for at least one month.

- Dose does not exceed FDA approved labeling; AND
- The requested medication will not be used in combination with other products indicated for acute treatment of HAE attacks (e.g. Ruconest, Kalbitor, or Icatibant)
- For Commercial members ONLY, they must have a failure, contraindication or intolerance to Ruconest;
- MMP members who have previously received this medication within the past 365 days are not subject to Step Therapy Requirements.

Continuation of Therapy Criteria:

- Patient continues to meet initial criteria; AND
- Patient has experienced reduction in severity and duration of attacks since starting treatment; AND
- Documentation supporting a positive clinical response to therapy with Berinert (e.g., chart notes, medical records)

Coverage durations:

- Initial coverage: 6 months
- Continuation of therapy coverage: 6 months

Per §§ 42 CFR 422.101, this clinical medical policy only applies to INTEGRITY in the absence of National Coverage Determination (NCD) or Local Coverage Determination (LCD).

Dosage/Administration:

Indication	Dose	Maximum dose (1 billable unit = 10 IU)
HAE	20 international units (IU) per kg body weight by intravenous injection upon recognition of an HAE attack.	1100 billable units per 28 days

Investigational use: All therapies are considered investigational when used at a dose or for a condition other than those that are recognized as medically accepted indications as defined in any one of the following standard reference compendia: American Hospital Formulary Service Drug information (AHFS-DI), Thomson Micromedex DrugDex, Clinical Pharmacology, Wolters Kluwer

Lexi-Drugs, or Peer-reviewed published medical literature indicating that sufficient evidence exists to support use. Neighborhood does not provide coverage for drugs when used for investigational purposes.

Applicable Codes:
Below is a list of billing codes applicable for covered treatment options. The below tables are provided for reference purposes and may not be all-inclusive. Requests received with codes from tables below do not guarantee coverage. Requests must meet all criteria provided in the procedure section.

The following HCPCS/CPT codes are:

HCPCS/CPT Code	Description
J0597	Injection, C-1 esterase inhibitor (human) Berinert, 10 units

References:

1. Berinert [package insert]. Kankakee, IL: CSL Behring LLC; September 2021. Accessed November 2023.
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4. 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: In Practice*. 2013; 1(5): 458-467.
5. 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.
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7. Lang DM, Aberer W, Bernstein JA, et al. International consensus on hereditary and acquired angioedema. *Ann Allergy Asthma Immunol*. 2012; 109:395-202.
8. 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.
9. 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.
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12. 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.