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, 08/28/2024, 12/04/2024, 06/25/2025, 11/10/2025		

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

Scope: Medicaid*, Commercial, Medicare
*(Medication only available on the Medical Benefit)

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.

Summary of Evidence

Berinert is a plasma derived C1 Esterase Inhibitor (Human) indicated for the treatment of acute abdominal, facial, or laryngeal hereditary angioedema (HAE) attacks in adult and pediatric patients. Clinical trials evaluating the efficacy and safety of Berinert in patients with acute HAE attacks have consistently demonstrated its effectiveness in rapidly relieving symptoms and reducing the duration of attacks. Key findings from pivotal trials have shown that Berinert, administered as an intravenous infusion, leads to a significant improvement in symptoms, including reduction in swelling, pain, and discomfort associated with HAE attacks. Adverse events associated with Berinert are rare and generally mild, with the most common being infusion-related reactions; however, these can be managed with appropriate premedication and monitoring.

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 management of HAE; 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

- Member 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) pathogenic variant as confirmed by genetic testing, OR
        - Member has a documented family history of angioedema and the member's angioedema was refractory to a trial of high-dose antihistamine therapy (e.g., cetirizine 40 mg per day or the equivalent) for at least one month; AND
- The requested medication will not be used in combination with other products indicated for acute treatment of HAE attacks (e.g. Ekterly (sebetralstat), Kalbitor (ecallantide), or Ruconest (C1 esterase inhibitor),or Icatibant); AND
- Other causes of angioedema have been ruled out (e.g., angiotensin-converting enzyme inhibitor [ACE-I] induced an angioedema, angioedema related to an estrogen containing drug, allergic angioedema); AND
- For Commercial and Medicaid members ONLY, they must have a failure, contraindication or intolerance to Ruconest; AND
- Medicare members who have previously received this medication within the past 365 days are not subject to Step Therapy Requirements.

Continuation of Therapy Criteria:

- Member continues to meet initial criteria; AND
- Documentation that the member has experienced reduction in severity and duration of attacks since starting treatment; AND
- Prophylaxis treatment should be considered based on the attack frequency, attack severity, comorbid conditions, and member's quality of life

Coverage durations:

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

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

Policy Rationale:
Berinert was reviewed by the Neighborhood Health Plan of Rhode Island Pharmacy & Therapeutics (P&T) Committee. Neighborhood adopted the following clinical coverage criteria to ensure that its members use Berinert according to Food and Drug Administration (FDA) approved labeling and/or relevant clinical literature. Neighborhood worked with network prescribers and pharmacists to draft these criteria. These criteria will help ensure its members are using this drug for a medically accepted indication, while minimizing the risk for adverse effects and ensuring more cost-effective options are used first, if applicable and appropriate. For Medicare members, these coverage criteria will only apply in the absence of National Coverage Determination (NCD) or Local Coverage Determination (LCD) criteria. Neighborhood will give individual consideration to each request it reviews based on the information submitted by the prescriber and other information available to the plan.

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:

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