

Berinert® (C1 Esterase Inhibitor, Human) (Intravenous)

Document Number: IC-0018

Last Review Date: 03/31/2023

Date of Origin: 11/28/2011

Dates Reviewed: 12/2011, 01/2013, 08/2013, 06/2014, 09/2014, 03/2015, 06/2015, 09/2015, 12/2015, 03/2016, 06/2016, 09/2016, 12/2016, 03/2017, 06/2017, 09/2017, 12/2017, 03/2018, 06/2018, 10/2018, 10/2019, 03/2020, 10/2020, 10/2021, 10/2022, 04/2023

I. Length of Authorization

Coverage will be provided for 12 weeks and is eligible for renewal (unless otherwise specified).

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 (unless otherwise specified).

II. Dosing Limits

A. Quantity Limit (max daily dose) [NDC Unit]:

- Berinert 500 IU single-dose vial: 22 vials every 28 days

B. Max Units (per dose and over time) [HCPCS Unit]:

- 1100 billable units per 28 days

III. Initial Approval Criteria ¹

Coverage is provided in the following conditions:

Universal Criteria ^{1,13,20}

- Must be prescribed by, or in consultation with, a specialist in: allergy, immunology, hematology, pulmonology, or medical genetics; **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**
 - Dipeptidyl peptidase IV (DPP-IV) inhibitors (e.g., sitagliptin); **AND**
 - Neprilysin inhibitors (e.g., sacubitril); **AND**

Treatment of acute abdominal, facial, or laryngeal attacks of Hereditary Angioedema (HAE) † 1,13,20,21,22

- 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 a HAE subtype§, which must be confirmed by repeat blood testing (treatment for acute attack should not be delayed for confirmatory testing):

HAE I (C1-Inhibitor deficiency) § 13,20,21,22
• 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 ○ Acquired angioedema has been ruled out (i.e., patient onset of symptoms occur prior to 30 years old, normal C1q levels, patient does not have underlying disease such as lymphoma or benign monoclonal gammopathy [MGUS], etc.)
HAE II (C1-Inhibitor dysfunction) § 20,22
• 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) § 20,21,22
• Normal C1-INH antigenic level; AND • Normal C4 level; AND • Normal C1-INH functional level; AND • Repeat blood testing <u>during an attack</u> 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 angiotensinogen gene, mutation in the plasminogen gene, mutation in the kininogen 1 gene, mutation in the myoferlin gene, mutation in the heparan sulfate 3-O-sulfotransferase 6 gene, etc.); OR ○ Patient has a family history of HAE and documented evidence of lack of efficacy of chronic high-dose antihistamine therapy (<i>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</i>) AND corticosteroids with or without omalizumab

† FDA Approved Indication(s)

IV. Renewal Criteria ¹

Coverage can be renewed based upon the following criteria:

- Patient continues to meet the universal and other indication-specific relevant criteria identified in section III; **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: severe hypersensitivity reactions, serious thromboembolic events (arterial or venous), 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 (unless otherwise specified).

V. Dosage/Administration ¹

Indication	Dose
Acute Hereditary Angioedema (HAE) attack	Administer 20 international units (IU) per kg body weight by intravenous injection upon recognition of an HAE attack. **Note: Patients may self-administer Berinert after being instructed by their healthcare provider.

VI. Billing Code/Availability Information

HCPCS Code:

- J0597 – Injection, C-1 esterase inhibitor (human), berinert, 10 units; 1 billable unit = 10 units

NDC:

- Berinert 500 IU single-dose carton kit (containing a single-dose vial of Berinert and a 10 mL vial of Sterile Water for Injection): 63833-0825-xx

VII. References

1. Berinert [package insert]. Kankakee, IL; CSL Behring LLC; September 2021. Accessed March 2023.
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4. 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.

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17. Frank MM, Sargent JS, Kane MA, et al. Epsilon aminocaproic acid therapy of hereditary angioneurotic edema: a double-blind study. *N Engl J Med*. 1972;286:808-812.
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Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
D84.1	Defects in the complement system

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determination (NCD), Local Coverage Determinations (LCDs), and Local Coverage Articles (LCAs) may exist and compliance with these policies is required where applicable. They can be found at:

<https://www.cms.gov/medicare-coverage-database/search.aspx>. Additional indications may be covered at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCD/LCA): N/A

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	Applicable State/US Territory	Contractor
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto GBA, LLC
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA, LLC
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC

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Provides free aids and services to people with disabilities to communicate effectively with us, such as:

- Qualified sign language interpreters
- Written information in other formats (large print, audio, accessible electronic formats, other formats)

Provides free language services to people whose primary language is not English, such as:

- Qualified interpreters
- Information written in other languages

If you need these services, contact a Grievance Specialist.

If you believe that PCHP has failed to provide these services or discriminated in another way on the basis of race, color, national origin, age, disability, or sex, you can file a grievance with:

Grievance Specialist
PreferredOne Community Health Plan
PO Box 59052
Minneapolis, MN 55459-0052
Phone: 1.800.940.5049 (TTY: 763.847.4013)
Fax: 763.847.4010
customerservice@preferredone.com

You can file a grievance in person or by mail, fax, or email. If you need help filing a grievance, a Grievance Specialist is available to help you.

You can also file a civil rights complaint with the U.S. Department of Health and Human Services, Office for Civil Rights, electronically through the Office for Civil Rights Complaint Portal, available at <https://ocrportal.hhs.gov/ocr/portal/lobby.jsf>, or by mail or phone at:

U.S. Department of Health and Human Services
200 Independence Avenue, SW
Room 509F, HHH Building
Washington, D.C. 20201
1-800-368-1019, 800-537-7697 (TDD)

Complaint forms are available at <http://www.hhs.gov/ocr/office/file/index.html>.

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PreferredOne Insurance Company
PO Box 59212
Minneapolis, MN 55459-0212
Phone: 1.800.940.5049 (TTY: 763.847.4013)
Fax: 763.847.4010
customerservice@preferredone.com

You can file a grievance in person or by mail, fax, or email. If you need help filing a grievance, a Grievance Specialist is available to help you.

You can also file a civil rights complaint with the U.S. Department of Health and Human Services, Office for Civil Rights, electronically through the Office for Civil Rights Complaint Portal, available at <https://ocrportal.hhs.gov/ocr/portal/lobby.jsf>, or by mail or phone at:

U.S. Department of Health and Human Services
200 Independence Avenue, SW
Room 509F, HHH Building
Washington, D.C. 20201
1-800-368-1019, 800-537-7697 (TDD)

Complaint forms are available at <http://www.hhs.gov/ocr/office/file/index.html>.

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