Medical Policy:

Berinert® (C1 esterase inhibitor, human) Intravenous

POLICY NUMBER	LAST REVIEW	ORIGIN DATE
MG.MM.PH.330	April 1, 2024	

The treating physician or primary care provider must submit to EmblemHealth, or ConnectiCare, as applicable (hereinafter jointly referred to as "EmblemHealth"), the clinical evidence that the member meets the criteria for the treatment or surgical procedure. Without this documentation and information, EmblemHealth will not be able to properly review the request preauthorization or post-payment review. The clinical review criteria expressed below reflects how EmblemHealth determines whether certain services or supplies are medically necessary. This clinical policy is not intended to pre-empt the judgment of the reviewing medical director or dictate to health care providers how to practice medicine. Health care providers are expected to exercise their medical judgment in rendering appropriate care. Health care providers are expected to exercise their medical judgment in rendering appropriate care.

EmblemHealth established the clinical review criteria based upon a review of currently available clinical information (including clinical outcome studies in the peer reviewed published medical literature, regulatory status of the technology, evidence-based guidelines of public health and health research agencies, evidence-based guidelines and positions of leading national health professional organizations, views of physicians practicing in relevant clinical areas, and other relevant factors). EmblemHealth expressly reserves the right to revise these conclusions as clinical information changes and welcomes further relevant information. Each benefit program defines which services are covered. The conclusion that a particular service or supply is medically necessary does not constitute a representation or warranty that this service or supply is covered and/or paid for by EmblemHealth, as some programs exclude coverage for services or supplies that EmblemHealth considers medically necessary.

If there is a discrepancy between this guideline and a member's benefits program, the benefits program will govern. Identification of selected brand names of devices, tests and procedures in a medical coverage policy is for reference only and is not an endorsement of any one device, test or procedure over another. In addition, coverage may be mandated by applicable legal requirements of a state, the Federal Government or the Centers for Medicare & Medicaid Services (CMS) for Medicare and Medicaid members. All coding and web site links are accurate at time of publication.

EmblemHealth may also use tools developed by third parties, such as the MCG™ Care Guidelines, to assist us in administering health benefits. The MCG™ Care Guidelines are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice. EmblemHealth Services Company, LLC, has adopted this policy in providing management, administrative and other services to EmblemHealth Plan, Inc., EmblemHealth Insurance Company, EmblemHealth Services Company, LLC, and Health Insurance Plan of Greater New York (HIP) related to health benefit plans offered by these entities. ConnectiCare, an EmblemHealth company, has also adopted this policy. All of the aforementioned entities are affiliated companies under common control of EmblemHealth Inc.

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.

Dosing Limits [Medical Benefit]

Max Units (per dose and over time):

1100 billable units per 28 days

Guideline

I. Initial Approval Criteria

1. <u>Treatment of acute abdominal, facial, or laryngeal attacks of Hereditary Angioedema (HAE) †</u>

A. Must be prescribed by, or in consultation with, a specialist in: allergy, immunology, hematology, pulmonology, or medical genetics; **AND**
B. Confirmation the patient is avoiding the following possible triggers for HAE attacks:
   i. Estrogen-containing oral contraceptive agents AND hormone replacement therapy; **AND**
   ii. Antihypertensive agents containing ACE inhibitors; **AND**
   iii. Dipeptidyl peptidase IV (DPP-IV) inhibitors (e.g., sitagliptin); **AND**
   iv. Neprilysin inhibitors (e.g., sacubitril); **AND**
C. 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**
D. 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)
1. 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** 2. Low C4 level (C4 below the lower limit of normal as defined by the laboratory performing the test); **AND** 3. Low C1-INH functional level (C1-INH functional level below the lower limit of normal as defined by the laboratory performing the test); **AND** a. Patient has a family history of HAE; **OR** b. Onset of HAE symptoms occurred before age 30; **OR** c. Normal C1q level
HAE II (C1-Inhibitor dysfunction)
1. Normal to elevated C1-INH antigenic level; **AND** 2. Low C4 level (C4 below the lower limit of normal as defined by the laboratory performing the test); **AND** 3. 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)
1. Normal C1-INH antigenic level; **AND** 2. Normal C4 level; **AND** 3. Normal C1-INH functional level; **AND** 4. Repeat blood testing during an attack has confirmed the patient does not have abnormal lab values indicative of HAE I or HAE II; **AND** 5. Either of the following: a. Patient has a known HAE-causing mutation (e.g., mutation of coagulation factor XII gene [F12 mutation], mutation in the angiopoietin-1 gene, mutation in the plasminogen gene, etc.); **OR** b. 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)

II. Renewal Criteria

1. Patient continues to meet the criteria above; **AND**
2. Significant improvement in severity and duration of attacks have been achieved and sustained; **AND**

3. Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include the following: hypersensitivity reactions, serious thrombotic events, laryngeal HAE attacks, etc.; **AND**
4. 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.

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

Berinert® (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

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

Applicable NDCs

Code	Description
63833-0825-xx	Berinert 500 IU single-use vial

ICD-10 Diagnoses

Code	Description
D84.1	Defects in the complement system

Revision History

Company(ies)	DATE	REVISION
EmblemHealth & ConnectiCare	4/1/2024	Annual Review: removed age restriction of “at least 6 years of age”
EmblemHealth & ConnectiCare	7/25/2023	Annual Review: Treatment of acute abdominal, facial, or laryngeal attacks of Hereditary Angioedema (HAE) † Initial Criteria: Added **“**Dipeptidyl peptidase IV (DPP-IV) inhibitors (e.g., sitagliptin); **AND** Neprilysin inhibitors (e.g., sacubitril); **AND”**
EmblemHealth & ConnectiCare	3/17/2022	Transferred policy to new template

References

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