Geisinger

POLICIES AND PROCEDURE MANUAL

Policy: MBP 85.0

Section: Medical Benefit Pharmaceutical Policy

Subject: Cinryze (C1 esterase inhibitor, human)

Applicable line of business:

Commercial	X	Medicaid	
Medicare	X	ACA	X
CHIP	X		

I. Policy:
Cinryze (C1 esterase inhibitor, human)

II. Purpose/Objective:
To provide a policy of coverage regarding Cinryze (C1 esterase inhibitor, human)

III. Responsibility:
A. Medical Directors
B. Medical Management
C. Pharmacy Department

IV. Required Definitions
1. Attachment – a supporting document that is developed and maintained by the policy writer or department requiring/authoring the policy.
2. Exhibit – a supporting document developed and maintained in a department other than the department requiring/authoring the policy.
3. Devised – the date the policy was implemented.
4. Revised – the date of every revision to the policy, including typographical and grammatical changes.
5. Reviewed – the date documenting the annual review if the policy has no revisions necessary.

V. Additional Definitions
Medical Necessity or Medically Necessary means Covered Services rendered by a Health Care Provider that the Plan determines are:
a. appropriate for the symptoms and diagnosis or treatment of the Member's condition, illness, disease or injury;
b. provided for the diagnosis and the direct care and treatment of the Member's condition, illness disease or injury;
c. in accordance with current standards good medical treatment practiced by the general medical community;
d. not primarily for the convenience of the Member, or the Member's Health Care Provider; and
e. the most appropriate source or level of service that can safely be provided to the Member. When applied to hospitalization, this further means that the Member requires acute care as an inpatient due to the nature of the services rendered or the Member's condition, and the Member cannot receive safe or adequate care as an outpatient

DESCRIPTION:
Cinryze (C1 esterase inhibitor, human) is believed to suppress contact system activation via inactivation of plasma kallikrein and factor XIIa, thus preventing bradykinin production. Unregulated bradykinin production is thought to contribute to the increased vascular permeability and angioedema.

CRITERIA FOR USE: Requires Prior Authorization by Medical Director or Designee

GRANDFATHER PROVISION – Members already established on therapy are eligible for approval as long as there is medical record documentation that the safety and effectiveness of use for the prescribed indication is supported by Food and Drug Administration (FDA) approval or adequate medical and scientific evidence in the medical literature

Cinryze (C1 esterase inhibitor, human) will be considered medically necessary for the commercial, exchange, CHIP, and Medicare lines of business for prophylaxis against attacks of hereditary angioedema when the following criteria are met:

- Member is 6 years of age or older **AND**
- Prescription is written by an allergist, immunologist, hematologist or dermatologist **AND**
- Medication is being used as prophylactic therapy for HAE attacks **AND**
- Diagnosis of hereditary angioedema has been established and supported by physician provided documentation of:
    - Recurrent, self-limiting non-inflammatory subcutaneous angioedema without urticaria, lasting more than 12 hours **OR**
    - Laryngeal edema **OR**
    - Recurrent, self-remitting abdominal pain lasting more than 6 hours, without clear organic etiology

AND

- The presence of specific abnormalities in complement proteins, in the setting of a suggestive clinical history of episodic angioedema without urticaria; supported by
    - Medical record documentation of 2 or more sets of complement studies, separated by one month or more, showing consistent results of
        - Low C4 levels **AND**
        - Less than 50% of the lower limit of normal C1-INH antigenic protein levels **OR**
        - Less than 50% of the lower limit of normal C1-INH function levels

AND

- Physician provided documentation of history of more than one (1) severe event per month OR a history of laryngeal attacks

QUANTITY LIMIT: 10 doses per 30 days.

AUTHORIZATION DURATION: Initial approval will be for 6 months or less if the reviewing provider feels it is medically appropriate. Subsequent approvals will be for an additional 6 months or less if the reviewing provider feels it is medically appropriate and will require medical record documentation of continued disease improvement or lack of disease progression. The medication will no longer be covered if patient experiences toxicity or worsening of disease.

Comparison of complement studies in angioedema disorders

Angiodema disorder	C4*	C1 inhibitor level	C1 inhibitor function	C1q	C3	Other tests (not routinely needed for diagnosis)
HAE I	Low	Low	Low (usually <50 percent of normal)	Normal	Normal	Genetic testing
HAE II	Low	Normal or elevated	Low (usually <50 percent of normal)	Normal	Normal	Genetic testing
HAE III	Normal	Normal	Normal	Normal	Normal	Mutations in gene for factor XII detected in some patients
AAE	Low	Normal or low	Low (usually <50 percent of normal)	Normal or low•	Normal or low	Anti-C1 inhibitor antibodies
Idiopathic angioedema	Normal	Normal	Normal	Normal	Normal	

LINE OF BUSINESS:
Eligibility and contract specific benefit limitations and/or exclusions will apply. Coverage statements found in the line of business specific benefit document will supersede this policy.

REFERENCES:

1. Cinryze [prescribing information]. Lexington, MA: Takeda Pharmaceuticals USA Inc; November 2024.
2. Busse, PJ, Christiansen SC, Riedl MA, et al. US HAEA Medical Advisory Board 2020 Guidelines for the Management of Hereditary Angioedema. US Hereditary Angioedema Association. Journal of Allergy clinical immunology Practice; 2020; 9(1):132-150 [cited 2023 Dec 27]. Available from: https://www.haea.org/pages/p/treatment_guidelines

This policy will be revised as necessary and reviewed no less than annually.

Devised: 9/8/10

Revised: 12/12, 08/14, 3/24/15 (criteria, QL) 5/15/15 (medically necessary), 3/6/19 (pediatrics per DHS), 1/17/23 (LOB carve out), 11/7/23 (danazol del June P&T, combined LOB criteria, formatting, Medicaid Business Segment), 12/31/23 (references added), 11/5/24 (Description, LOB table, taglines, removed Medicaid business segment)

Reviewed: 10/11; 12/13, 08/14, 3/16, 3/30/17, 3/29/18, 1/30/19, 1/10/20, 1/19/21, 1/18/22, 9/18/25

MA UM Committee approval: 12/31/23, 5/22/24, 10/27/25