C1 Esterase Inhibitor (Human) (Cinryze®)

NDC CODE(S) 42227-0081-XX CINRYZE 500UNIT Solution Reconstituted (VIROPHARMA ,INC)

DESCRIPTION

C1 esterase inhibitor (C1-INH) is a normal constituent of human blood and is a serine proteinase inhibitor or serpin. C1-INH's primary function is to regulate the activation of the complement and intrinsic coagulation pathway. It also has a role in regulation of the fibrinolytic system.

Individuals with an inherited deficiency of C1-INH suffer from sudden, recurrent edematous swellings of the subcutaneous or submucosal tissues. This condition is known as hereditary angioedema (HAE).

Commercially, C1-INH is available in two forms, those derived from purified human plasma which has undergone multiple viral reduction steps and a recombinant analogue purified from the milk of transgenic rabbits. Cinryze® is a human plasma-derived product formulated for prevention of angioedema attacks.

POLICY

- C1 Esterase Inhibitor - Cinryze® for the prevention of angioedema attacks of Hereditary Angioedema (HAE) is considered ***medically necessary*** if the medical appropriateness criteria are met. **(See Medical Appropriateness below.)**

- C1 Esterase Inhibitor - Cinryze® for the treatment or prevention of other conditions/diseases is considered ***investigational***

MEDICAL APPROPRIATENESS

INITIAL APPROVAL

- C1 Esterase Inhibitor - Cinryze® is considered **medically appropriate** if **ALL** of the following criteria are met:
  - Individual is 6 years of age or older
  - Not used in combination with other prophylactic therapies targeting C1 inhibitor or kallikrein (e.g., Haegarda® or Takhzyro™)
  - Confirmation of avoidance of the following possible triggers of HAE attacks:
    - Estrogen-containing oral contraceptive agents **AND** hormone replacement therapy
    - Antihypertensive agents containing ACE inhibitors
    - Dipeptidyl peptidase IV (DPP-IV) inhibitors (e.g., sitagliptin)
    - Neprilysin inhibitors (e.g., sacubitril)
  - Individual has **ANY 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) if **ALL** of the following:
      - 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)
      - Low C4 level (C4 below the lower limit of normal as defined by the performing lab)
      - C1-INH functional level low (C1-INH functional level below the lower limit of normal as defined by the performing lab) and **ANY ONE** of the following:
        - Individual positive family history of HAE

- Acquired angioedema has been ruled out (i.e., onset of symptoms occur prior to 30 years old, normal C1q levels, individual does not have underlying disease such as lymphoma or benign monoclonal gammopathy [MGUS], etc.)
- **HAE II (C1-Inhibitor dysfunction)** if **ALL** of the following:
  - Normal to elevated C1-INH antigenic level
  - Low C4 level (C4 below the lower limit of normal as defined by the performing lab)
  - Low C1-INH functional level (C1-INH functional level below the lower limit of normal as defined by the performing lab)
- **HAE with normal C1-INH (formerly known as HAE III)** prophylaxis for HAE with normal C1-INH is not routinely recommended and will be evaluated on a case by case basis

- Individual has **ANY ONE** of the following:
  - Individual is receiving treatment as short-term HAE prophylaxis prior to a procedure (i.e. dental or medical procedure)
  - Individual has history of **ANY ONE** of the following criteria for long-term HAE prophylaxis:
    - History of two (2) or more severe HAE attacks per month (e.g., airway swelling, debilitating cutaneous or gastrointestinal episodes)
    - Individual disabled more than five days per month by HAE attacks
    - History of at least one laryngeal attack caused by HAE
- "On demand" HAE therapy (e.g., Kalbitor®, Firazyr®, Berinert®, Ruconest®) does not offer satisfactory control or access to "on-demand therapy" is limited

RENEWAL CRITERIA

- C1 Esterase Inhibitor - Cinryze® is considered **medically appropriate** for renewal if **ALL** of the following criteria are met:
  - Individual continues to meet initial approval criteria
  - Absence of unacceptable toxicity from the drug, Examples of unacceptable toxicity include the following: severe hypersensitivity reactions, serious thromboembolic events (arterial and venous), etc. and **ANY ONE** of the following:
    - Significant improvement in severity and duration of attacks have been achieved and sustained
    - Individual requires dose titration due to an inadequate response to therapy (> 1.0 HAE attack/month, regardless of severity/duration)

INDICATION(S)	DOSAGE & ADMINISTRATION
Prophylaxis of Hereditary Angioedema (HAE) attacks	**Adult/adolescents (at least >12 years of age)** 1,000 units by intravenous injection every 3 to 4 days *For patients who have not responded adequately to initial dosing, doses up to 2,500 U (not exceeding 100 U/kg) every 3 or 4 days may be considered based on individual patient response.* **Pediatric patients (6 to 11 years of age)** 500 units by intravenous injection every 3 to 4 days *The dose may be adjusted according to individual patient response, up to 1,000 U every 3 to 4 days*.

LENGTH OF AUTHORIZATION

Coverage will be provided for 12 months and may be renewed.

Refer to **DOSAGE LIMITS** below

APPLICABLE TENNESSEE STATE MANDATE REQUIREMENTS

BlueCross BlueShield of Tennessee's Medical Policy complies with Tennessee Code Annotated Section 56-7-2352 regarding coverage of off-label indications of Food and Drug Administration (FDA) approved drugs when the off-label use is recognized in one of the statutorily recognized standard reference compendia or in the published peer-reviewed medical literature.

IMPORTANT REMINDER

We develop Medical Policies to provide guidance to Members and Providers. This Medical Policy relates only to the services or supplies described in it. The existence of a Medical Policy is not an authorization, certification, explanation of benefits or a contract for the service (or supply) that is referenced in the Medical Policy. For a determination of the benefits that a Member is entitled to receive under his or her health plan, the Member's health plan must be reviewed. If there is a conflict between the Medical Policy and a health plan, the express terms of the health plan will govern.

ADDITIONAL INFORMATION

For appropriate chemotherapy regimens, dosage information, contraindications, precautions, warnings, and monitoring information, please refer to one of the standard reference compendia (e.g., the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) published by the National Comprehensive Cancer Network®, Drugdex Evaluations of Micromedex Solutions at Truven Health, or The American Hospital Formulary Service Drug Information).

SOURCES

Betschel, S., Badiou, J., Binkley, K., Borici-Mazi, R., Hébert, J., Kanani, A., et al. (2019). The International/Canadian Hereditary Angioedema Guideline. Allergy, Asthma & Clinical Immunology. 2019. 15:72. Published online 2019 Nov 25. doi: 10.1186/s13223-019-0376-8.

Bowen, T., Cicardi, M., Farkas, H., Bork, K., Longhurst, H. J., Zuraw, B., et al. (2010). International consensus algorithm for the diagnosis, therapy and management of hereditary angioedema. *Allergy Asthma & Clinical Immunology*; 6 (1), 24.

Lexi-Comp Online. (2020, March). AHFS DI. *C1 Esterase Inhibitor*. Retrieved November 9, 2020 from Lexi-Comp Online with AHFS.

Maurer, M., Magerl, M., Ansotegui, I., Ayg€oren-P€urs€un, E., Betschel, S., Bork, K., et al. (2018). The international WAO/EAACI guideline for the management of hereditary angioedema-The 2017 revision and update. *Allergy,* 73 (8), 1575–1596.

MICROMEDEX Healthcare Series. Drugdex Evaluations. (2020, September). *C1 Esterase Inhibitor*. Retrieved November 9, 2020 from MICROMEDEX Healthcare Series.

U. S. Food and Drug Administration. (2018, June). Center for Biologics Evaluation and Research. *Cinryze® C1 Esterase Inhibitor (Human) label.* Retrieved November 9, 2020 from http://www.fda.gov/downloads/BiologicsBloodVaccines/BloodBloodProducts/ApprovedProducts/LicensedProductsBLAs/FractionatedPlasmaProducts/UCM129918.pdf.

EFFECTIVE DATE 4/2/21

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