Pharmacy Medical Necessity Guidelines: Cinryze® (C1 Esterase Inhibitor [Human])

Effective: July 1, 2020

Prior Authorization Required	√	Type of Review – Care Management	
Not Covered		Type of Review – Clinical Review	√
Pharmacy (RX) or Medical (MED) Benefit	MED	Department to Review	PRECERT / MM

These pharmacy medical necessity guidelines apply to the following:

Commercial Products

☒ Tufts Health Plan Commercial products – large group plans
☒ Tufts Health Plan Commercial products – small group and individual plans
☒ Tufts Health Freedom Plan products – large group plans
☒ Tufts Health Freedom Plan products – small group plans
- CareLink℠ – Refer to CareLink Procedures, Services and Items Requiring Prior Authorization

Tufts Health Public Plans Products

☒ Tufts Health Direct – A Massachusetts Qualified Health Plan (QHP) (a commercial product)
☒ Tufts Health Together – MassHealth MCO Plan and Accountable Care Partnership Plans
☒ Tufts Health RITogether – A Rhode Island Medicaid Plan

Fax Numbers:

All plans except Tufts Health Public Plans:
PRECERT:617.972.9409

Tufts Health Public Plans:
MM: 888.415.9055

Note: This guideline does not apply to Medicare Members (includes dual eligible Members).

OVERVIEW

FOOD AND DRUG ADMINISTRATION-APPROVED INDICATIONS

Cinryze is a C1 esterase inhibitor indicated for routine prophylaxis against angioedema attacks in adults, adolescents, and pediatric patients (6 years of age and older) with Hereditary Angioedema (HAE).

Hereditary angioedema is a rare, episodic, autosomal dominant, swelling disorder that is characterized by C1 esterase inhibitor (C1-INH) deficiency. C1-INH coordinates the activation of the complement, contact, and fibrinolytic systems. A reduction in the activity of C1-INH may result in an elevated level of bradykinin, which is a key mediator in HAE symptoms. Patients with HAE may experience attacks of swelling and inflammation in the extremities, abdomen, face, urogenital tract, and/or the larynx that are random, recurrent, and potentially life-threatening. The age of onset is variable, ranging from early childhood to adult, with a worsening in frequency occurring around puberty. The age of onset can help to differentiate between HAE and acquired angioedema (AAE), which normally does not present until the fourth decade of life.

Treatment of HAE is divided into acute treatment, short-term/procedural prophylaxis to prevent an attack, and long-term/routine prophylaxis to minimize the frequency and severity of attacks. Long-term prophylaxis is recommended for patients who experience more than one attack per month, or for those who feel the condition is significantly impacting their lives. Short-term prophylaxis is recommended before dental procedures, minor surgery, endoscopy, or any situation where trauma may precipitate an attack; however, there are no FDA-approved agents currently available for procedural prophylaxis. A multifaceted approach that uses both pharmacologic and supportive therapies is required for optimal prevention and treatment of HAE.

COVERAGE GUIDELINES

The plan may authorize coverage of Cinryze (C1 esterase inhibitor) for Members when all of the following criteria are met:

Initial Therapy

1. Documented diagnosis of hereditary angioedema by an immunologist or allergist

AND

2. Documentation that "on-demand" therapy (e.g., icatibant, Kalbitor, Ruconest, or Berinert) did not provide satisfactory control or access to "on-demand" therapy is limited

AND

3. Documentation the Member is NOT concurrently taking an angiotensin converting enzyme (ACE) inhibitor or estrogen replacement therapy

AND

4. Documentation the Member has had an insufficient response or contraindication to both of the following classes of medication:
    a. 17α–alkylated androgens (e.g., danazol, stanozolol, oxandrolone, methyltestosterone)
    b. Antifibrinolytic agents (e.g., aminocaproic acid, tranexamic acid)

Reauthorization Criteria

1. The prescribing physician is an immunologist or allergist

AND

2. Documentation of improvement in severity and duration of attacks has been achieved and sustained

LIMITATIONS

- Cinryze (C1 esterase inhibitor) will be authorized for 12 months.
- Members new to the plan stable on Cinryze (C1 esterase inhibitor) should be reviewed against Initial Therapy coverage criteria.

CODES

The following HCPCS/CPT code(s) are:

Code	Description
J0598	Injection, C1 esterase inhibitor (human), 10 units

REFERENCES

1. Bernstein JA, Manning ME, Li H, et al. Escalating doses of C1 esterase inhibitor (CINRYZE) for prophylaxis in patients with hereditary angioedema. *J Allergy Clin Immunol Pract*. 2014 Jan-Feb;2(1):77-84.
2. Bowen T, Cicardi M, Farkas H, et al. 2010 International consensus algorithm for the diagnosis, therapy, and management of hereditary angioedema. *Allergy Asthma Clin Immunol*. 2010;6(1):24.
3. Cinryze (C1 Esterase Inhibitor [Human]) [package insert]. Exton, PA: ViroPharma Inc., June 2018.
4. Craig TJ, Levy RJ, Wasserman RL et al. Efficacy of human C1 esterase inhibitor concentrate compared with placebo in acute hereditary angioedema attacks. *J Allergy Clin Immunol*. Oct 2009;124(4):801-808.
5. Craig T, Riedl M, Dykewicz MS et al. When is prophylaxis for hereditary angioedema necessary? *Ann Allergy Asthma Immunol*. 2009; 102:366-72.
6. Epstein TG, Bernstein JA. Current and emerging management options for hereditary angioedema in the US. *Drugs*. 2008; 68(18):2561-73.
7. Frank, MM. Hereditary angioedema: the clinical syndrome and its management in the United States. *Immunol Allergy Clin North Am*. 2006; 26(4):653-68.
8. Frank, MM. Hereditary angioedema. *J Allergy Clin Immunol*. 2008; 121(2 Suppl):S398-401.
9. Kreuz W, Martinez-Saguer I, Aygören-Pürsün E et al. C1-inhibitor concentrate for individual replacement therapy in patients with severe hereditary angioedema refractory to danazol prophylaxis. *Transfusion*. 2009 Sep;49(9):1987-95.
10. Kunschak M, Engl W, Maritsch F et al. A randomized, controlled trial to study the efficacy and safety of C1 inhibitor concentrate in treating hereditary angioedema. *Transfusion*. 1998 Jun;38(6):540-9.
11. Lyseng-Williamson KA. Nanofiltered human C1 inhibitor concentrate (Cinryze®): in hereditary angioedema. *BioDrugs*. 2011 Oct 1;25(5):317-27.
12. Sachse MM, Khachemoune A, Guldbakke KK et al. Hereditary angioedema. *J Drugs Dermatol*. 2006; 5(9):848-52.
13. The US Hereditary Angioedema Association. For Healthcare Providers. URL: haea.org/professionals. Available from Internet. Accessed 2013 April 10.
14. U.S. National Library of Medicine. Genetics Home Reference. Hereditary angioedema. URL: ghr.nlm.nih.gov/condition/hereditary-angioedema. Accessed 2013 April 10.
15. Weis M. Clinical review of hereditary angioedema: diagnosis and management. *Postgrad Med J* 2009; 121(6):113-20.
16. Zuraw B. Hereditary angioedema. *N Engl J Med*. 2008;359;1027-1036.
17. Zuraw BL, Busse PJ, White M et al. Nanofiltered C1 inhibitor concentrate for treatment of hereditary angioedema. *N Engl J Med*. 2010 Aug 5;363(6):513-22.

18. Zuraw BL, Kalfus I. Safety and efficacy of prophylactic nanofiltered C1-inhibitor in hereditary angioedema. *Am J Med*. 2012 Sep;125(9):938.e1-7.

APPROVAL HISTORY

March 10, 2009: Reviewed by Pharmacy & Therapeutics Committee.

Subsequent endorsement date(s) and changes made:

1. July 14, 2009: Removed criterion, "The Member has a history of at least two HAE attacks per month." Removed criterion, "The Member has had an insufficient response or intolerance to corticosteroids and antihistamines." Added "immunologist" to criteria #1. Added criteria #2, 3, and 4
2. January 1, 2010: Removal of Tufts Medicare Preferred language (separate criteria have been created specifically for Tufts Medicare Preferred)
3. February 16, 2010: Administrative Update: Removed temporary and miscellaneous billing codes and replaced with code J0598
4. July 13, 2010: No changes.
5. July 12, 2011: No changes.
6. June 12, 2012: No changes.
7. May 14, 2013: No changes.
8. April 8, 2014: No changes.
9. April 14, 2015: No changes.
10. January 1, 2016: Administrative change to rebranded template
11. March 8, 2016: No changes.
12. April 12, 2016: Effective 10/01/2016, Medical Necessity Guideline applies to Tufts Health Together.
13. April 11, 2017: Administrative update. Effective 6/1/2017, Medical Necessity Guideline applies to Tufts Health RITogether.
14. March 13, 2018: No changes.
15. August 7, 2018: No changes.
16. February 12, 2019: No changes.
17. April 9, 2019: Added allergist as a provider specialty to the Medical Necessity Guideline.
18. February 11, 2020: Effective April 1, 2020, updated approval duration to 12 months and added Reauthorization criteria. Updated initial therapy criteria to remove documentation of a specific frequency and type of history of attacks. Documentation that "on-demand" therapy (e.g., icatibant, Kalbitor, Ruconest, or Berinert) did not provide satisfactory control or access to "on-demand" therapy is limited is required.

BACKGROUND, PRODUCT AND DISCLAIMER INFORMATION

Pharmacy Medical Necessity Guidelines have been developed for determining coverage for plan benefits and are published to provide a better understanding of the basis upon which coverage decisions are made. The plan makes coverage decisions on a case-by-case basis considering the individual member's health care needs. Pharmacy Medical Necessity Guidelines are developed for selected therapeutic classes or drugs found to be safe, but proven to be effective in a limited, defined population of patients or clinical circumstances. They include concise clinical coverage criteria based on current literature review, consultation with practicing physicians in the service area who are medical experts in the particular field, FDA and other government agency policies, and standards adopted by national accreditation organizations. The plan revises and updates Pharmacy Medical Necessity Guidelines annually, or more frequently if new evidence becomes available that suggests needed revisions.

For self-insured plans, coverage may vary depending on the terms of the benefit document. If a discrepancy exists between a Pharmacy Medical Necessity Guideline and a self-insured Member's benefit document, the provisions of the benefit document will govern.

Treating providers are solely responsible for the medical advice and treatment of members. The use of this policy is not a guarantee of payment or a final prediction of how specific claim(s) will be adjudicated. Claims payment is subject to member eligibility and benefits on the date of service, coordination of benefits, referral/authorization and utilization management guidelines when applicable, and adherence to plan policies and procedures and claims editing logic.

Provider Services