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

Effective: April 11, 2017 (All plans except Tufts Health RITogether)
Effective: June 1, 2017 (Tufts Health RITogether)

Prior Authorization Required ✓

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<thead>
<tr>
<th>Type of Review – Care Management</th>
<th>Type of Review – Clinical Review ✓</th>
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<tbody>
<tr>
<td>MED / RX</td>
<td>PRECERT / MM / RXUM</td>
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Pharmacy (RX) or Medical (MED) Benefit
Department to Review

This Pharmacy Medical Necessity Guideline applies to the following:

Tufts Health Plan Commercial Plans
✓ Tufts Health Plan Commercial Plans – large group plans
✓ Tufts Health Plan Commercial Plans – small group and individual plans

Tufts Health Public Plans
✓ Tufts Health Direct – Health Connector
✓ Tufts Health Together – A MassHealth Plan
✓ Tufts Health RITogether – A RIte Care + Rhody Health Partners Plan

Tufts Health Freedom Plan products
✓ Tufts Health Freedom Plan - large group plans
✓ Tufts Health Freedom Plan - small group plans

Fax Numbers:
All plans except Tufts Health Public Plans:
PRECERT: 617-972-9409

Tufts Health Direct – Health Connector:
MM: 888-415-9055

Tufts Health Together – A MassHealth Plan:
RxUM: 617-673-0988

Note: For Tufts Health Plan Medicare Preferred Members, please refer to the Tufts Health Plan Medicare Preferred prior authorization criteria. Background, applicable product and disclaimer information can be found on the last page.

OVERVIEW

FOOD AND DRUG ADMINISTRATION-APPROVED INDICATIONS

Cinryze is a C1 esterase inhibitor indicated for routine prophylaxis against angioedema attacks in adolescent and adult patients with Hereditary Angioedema (HAE).

Hereditary angioedema (HAE) is a rare, life-threatening, autosomal dominant disease caused by the deficiency of the C1 inhibitor plasma protein, which controls inflammation. It is characterized by random episodes of disfiguring and painful swelling of the extremities, face, abdomen, urogenital tract and, laryngeal tract. Its prevalence is uncertain but is estimated to be approximately 1 case per 50,000 persons, without known differences among ethnic groups. Symptoms typically begin in childhood worsen around puberty, and persist throughout life, with unpredictable severity. Untreated patients have attacks every 7 to 14 days on average, with the frequency ranging from virtually never to every 3 days.

COVERAGE GUIDELINES

The plan may authorize coverage of Cinryze (C1 inhibitor) for Members, when ALL of the following criteria are met:
1. Documented diagnosis of hereditary angioedema by an immunologist

AND

2. The Member’s history of HAE attacks is consistent with at least ONE of the following criteria:
   a) One or more abdominal or respiratory attacks per month
   b) History of laryngeal attacks
   c) Requires emergency medical care 3 or more times per year

AND

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

AND

4. 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. ε – aminocaproic acid, tranexamic acid)
LIMITATIONS
None

CODES
The following HCPCS/CPT code(s) are:

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
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<tr>
<td>J0598</td>
<td>Injection, C1 esterase inhibitor (human), 10 units</td>
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REFERENCES

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

Subsequent endorsement date(s) and changes made:
- 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
- January 1, 2010: Removal of Tufts Medicare Preferred language (separate criteria have been created specifically for Tufts Medicare Preferred)
- February 16, 2010: Administrative Update: Removed temporary and miscellaneous billing codes and replaced with code J0598
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. They are used in conjunction with a Member’s benefit document and in coordination with the Member’s physician(s). 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.

This Pharmacy Medical Necessity Guideline does not apply to Uniformed Services Family Health Plan Members or to certain delegated service arrangements. Unless otherwise noted in the Member’s benefit document or applicable Pharmacy Medical Necessity Guideline, Pharmacy Medical Necessity Guidelines do not apply to CareLinkSM Members. For self-insured plans, drug coverage may vary depending on the terms of the benefit document. If a discrepancy exists between a coverage guideline and a self-insured Member’s benefit document, the provisions of the benefit document will govern. Applicable state or federal mandates will take precedence.

For Tufts Health Plan Medicare Preferred, please refer to Tufts Health Plan Medicare Preferred Prior Authorization Criteria.

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.