DRUG QUANTITY MANAGEMENT POLICY – PER DAYS

POLICY: Hereditary Angioedema – Ruconest Drug Quantity Management Policy – Per Days
- Ruconest® (recombinant C1 esterase inhibitor intravenous infusion – Pharming)

REVIEW DATE: 01/29/2025

INSTRUCTIONS FOR USE

THE FOLLOWING COVERAGE POLICY APPLIES TO HEALTH BENEFIT PLANS ADMINISTERED BY CIGNA COMPANIES. CERTAIN CIGNA COMPANIES AND/OR LINES OF BUSINESS ONLY PROVIDE UTILIZATION REVIEW SERVICES TO CLIENTS AND DO NOT MAKE COVERAGE DETERMINATIONS. REFERENCES TO STANDARD BENEFIT PLAN LANGUAGE AND COVERAGE DETERMINATIONS DO NOT APPLY TO THOSE CLIENTS. COVERAGE POLICIES ARE INTENDED TO PROVIDE GUIDANCE IN INTERPRETING CERTAIN STANDARD BENEFIT PLANS ADMINISTERED BY CIGNA COMPANIES. PLEASE NOTE, THE TERMS OF A CUSTOMER'S PARTICULAR BENEFIT PLAN DOCUMENT [GROUP SERVICE AGREEMENT, EVIDENCE OF COVERAGE, CERTIFICATE OF COVERAGE, SUMMARY PLAN DESCRIPTION (SPD) OR SIMILAR PLAN DOCUMENT] MAY DIFFER SIGNIFICANTLY FROM THE STANDARD BENEFIT PLANS UPON WHICH THESE COVERAGE POLICIES ARE BASED. FOR EXAMPLE, A CUSTOMER'S BENEFIT PLAN DOCUMENT MAY CONTAIN A SPECIFIC EXCLUSION RELATED TO A TOPIC ADDRESSED IN A COVERAGE POLICY. IN THE EVENT OF A CONFLICT, A CUSTOMER'S BENEFIT PLAN DOCUMENT ALWAYS SUPERSEDES THE INFORMATION IN THE COVERAGE POLICIES. IN THE ABSENCE OF A CONTROLLING FEDERAL OR STATE COVERAGE MANDATE, BENEFITS ARE ULTIMATELY DETERMINED BY THE TERMS OF THE APPLICABLE BENEFIT PLAN DOCUMENT. COVERAGE DETERMINATIONS IN EACH SPECIFIC INSTANCE REQUIRE CONSIDERATION OF 1) THE TERMS OF THE APPLICABLE BENEFIT PLAN DOCUMENT IN EFFECT ON THE DATE OF SERVICE; 2) ANY APPLICABLE LAWS/REGULATIONS; 3) ANY RELEVANT COLLATERAL SOURCE MATERIALS INCLUDING COVERAGE POLICIES AND; 4) THE SPECIFIC FACTS OF THE PARTICULAR SITUATION. EACH COVERAGE REQUEST SHOULD BE REVIEWED ON ITS OWN MERITS. MEDICAL DIRECTORS ARE EXPECTED TO EXERCISE CLINICAL JUDGMENT AND HAVE DISCRETION IN MAKING INDIVIDUAL COVERAGE DETERMINATIONS. COVERAGE POLICIES RELATE EXCLUSIVELY TO THE ADMINISTRATION OF HEALTH BENEFIT PLANS. COVERAGE POLICIES ARE NOT RECOMMENDATIONS FOR TREATMENT AND SHOULD NEVER BE USED AS TREATMENT GUIDELINES. IN CERTAIN MARKETS, DELEGATED VENDOR GUIDELINES MAY BE USED TO SUPPORT MEDICAL NECESSITY AND OTHER COVERAGE DETERMINATIONS.

CIGNA NATIONAL FORMULARY COVERAGE:

OVERVIEW

Ruconest, a recombinant C1 esterase inhibitor (C1-INH), is indicated for the **treatment of acute hereditary angioedema (HAE) attacks** in adults and adolescent patients.[1]

Dosing

The recommended dose of Ruconest is 50 units/kg, up to a maximum dose of 4,200 units administered as a slow intravenous injection over approximately five minutes.[1] If the attack symptoms persist, an additional dose can be administered at the recommended dose level. Do not exceed 4,200 units per dose. No more than two doses should be administered within a 24-hour period. Of note, in the clinical trial, rescue treatment with Ruconest was administered if a patient did not experience the beginning of relief within 4 hours after the first dose. The second rescue dose was only required for 11% of Ruconest-treated patients; most patients responded to a single dose.

Availability

Ruconest is supplied in single-use 25 mL glass vials containing 2,100 units of Ruconest as lyophilized powder for reconstitution.[1] Each carton contains one single-use vial.

Guidelines

US HAE Medical Advisory Board guidelines (2020) recommend that all patients with laboratory confirmed HAE should have access to at least two standard doses of an approved on-demand medication for treatment of acute attacks.[2] On-demand treatment of attacks is most effective when administered early after attack onset.

Additional Information

In the pivotal studies of Ruconest in patients with peripheral, abdominal, or oropharyngeal-laryngeal HAE attacks, at baseline (prior to Ruconest therapy), the mean number of attacks per year was 28 (range: 0 to 143) in Study 1 and 17 in Study 2.[3,4] The majority of patients were on prophylactic therapy. Additionally, in the open-label extension phase of Study 1, 97% of attacks were able to be successfully treated with only one dose of Ruconest 50 U/kg (up to a maximum of 4,200 units).[1] In a pooled post-hoc analysis of the pivotal trials, the vast majority of attacks (90.7%) responded to Ruconest treatment within 4 hours and only 7.1% of attacks treated with Ruconest reoccurred within 72 hours of initial treatment.

Based on the above data, the average patient is estimated to experience 2 to 3 attacks per month, but additional attacks may occur. The quantity limits outlined below provide for the patient to treat 4 attacks (at the maximum Ruconest dose) per 28 days, with an override provided to treat an additional 4 attacks (at the maximum Ruconest dose) each month.

POLICY STATEMENT

This Drug Quantity Management program has been developed to promote the safe, effective, and economic use of Ruconest. If the Drug Quantity Management rule is not met for the requested medication at the point of service, coverage will be determined by the Criteria below. "One-time" approvals are provided for 30 days in duration.

Drug Quantity Limits

Product	Package Size	Retail Maximum Quantity per 28 Days	Home Delivery Maximum Quantity per 84 Days
Ruconest® (recombinant C1 esterase inhibitor IV infusion)	2,100 unit single-dose vials	16 vials*	48 vials*

IV – Intravenous; * This is a quantity sufficient to treat four acute hereditary angioedema attacks in each 28-day period, assuming that the patient requires two doses in a 24-hour period to treat the attack. If a patient requires additional Ruconest doses for an additional attack, exceptions will be provided based on the criteria below.

Hereditary Angioedema – Ruconest Drug Quantity Management Policy – Per Days product(s) is(are) covered as medically necessary when the following criteria is(are) met. Any other exception is considered not medically necessary.

CRITERIA

1. If the patient requires additional doses of Ruconest to treat a subsequent attack of hereditary angioedema (HAE), approve a one-time override for 16 additional vials at retail or home delivery.
Note: At retail, the approval quantity should be the number of Ruconest vials the patient has received in the past 28 days plus 16 vials. At home delivery, the approval quantity should be the number of Ruconest vials the patient has received in the past 84 days plus 16 vials. ONE override may be approved ONCE every 30 days.

REFERENCES

1. Ruconest® intravenous infusion [prescribing information]. Warren, NJ: Pharming; April 2020.
2. Busse PJ, Christiansen SC, Riedl MA, et al. US HAEA Medical Advisory Board 2020 guidelines for the management of hereditary angioedema. *J Allergy Clin Immunol Pract*. 2021;9(1):132-150.e3.
3. Riedl MA, Bernstein JA, Li H, et al. Recombinant human C1-esterase inhibitor relieves symptoms of hereditary angioedema attacks: phase 3, randomized, placebo-controlled trial. *Ann Allergy Asthma Immunol.* 2014;112:163-169.
4. Zuraw B, Cicardi M, Levy RJ, et al. Recombinant human C1-inhibitor for the treatment of acute angioedema attacks in patients with hereditary angioedema. *J Allergy Clin Immunol.* 2010;126:821-827.
5. Bernstein JA, Relan A, Harper JR, etc. Sustained response of recombinant human C1 esterase inhibitor for acute treatment of hereditary angioedema attacks. *Ann Allergy Asthma Immunol*. 2017;118(4):452-455.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	No criteria changes.	02/09/2024
Early Annual Revision	Policy statement was updated to note that "one-time" approvals are provided for 30 days in duration. **Ruconest 2,100 unit single-dose vials:** Override was updated to approve a one-time override for 16 additional vials if the patient requires additional doses of Ruconest to treat a subsequent attack of hereditary angioedema. Previously, criteria approved 4 additional vials. Criteria Note updated to clarify "At retail, the approval quantity should be the number of Ruconest vials the patient has received in the past 28 days plus 16 vials. At home delivery, the approval quantity should be the number of Ruconest vials the patient has received in the past 84 days plus 16 vials. ONE override may be approved ONCE every 30 days."	01/29/2025