# DRUG QUANTITY MANAGEMENT POLICY – PER DAYS

**POLICY:** Hereditary Angioedema – Icatibant Drug Quantity Management Policy – Per Days
- Firazyr® (icatibant subcutaneous injection – Takeda, generic)
- Sajazir™ (icatibant subcutaneous injection – Cycle)

**REVIEW DATE:** 02/02/2026

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***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 WHERE APPROPRIATE AND HAVE DISCRETION IN MAKING INDIVIDUAL COVERAGE DETERMINATIONS. WHERE COVERAGE FOR CARE OR SERVICES DOES NOT DEPEND ON SPECIFIC CIRCUMSTANCES, REIMBURSEMENT WILL ONLY BE PROVIDED IF A REQUESTED SERVICE(S) IS SUBMITTED IN ACCORDANCE WITH THE RELEVANT CRITERIA OUTLINED IN THE APPLICABLE COVERAGE POLICY, INCLUDING COVERED DIAGNOSIS AND/OR PROCEDURE CODE(S). REIMBURSEMENT IS NOT ALLOWED FOR SERVICES WHEN BILLED FOR CONDITIONS OR DIAGNOSES THAT ARE NOT COVERED UNDER THIS COVERAGE POLICY (SEE "CODING INFORMATION" BELOW). WHEN BILLING, PROVIDERS MUST USE THE MOST APPROPRIATE CODES AS OF THE EFFECTIVE DATE OF THE SUBMISSION. CLAIMS SUBMITTED FOR SERVICES THAT ARE NOT ACCOMPANIED BY COVERED CODE(S) UNDER THE APPLICABLE COVERAGE POLICY WILL BE DENIED AS NOT COVERED. 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

Icatibant, a synthetic decapeptide, is indicated for the treatment of **acute hereditary angioedema (HAE) attacks** in adults ≥ 18 years of age.[1,2]

### Dosing

The recommended dose of icatibant is 30 mg administered by subcutaneous (SC) injection in the abdominal area.[1,2] Additional doses may be administered at intervals of at least 6 hours if response is inadequate or if symptoms recur. No more than three doses may be administered in any 24 hour period.

### Availability

Icatibant is supplied in a single-use, prefilled syringe for SC injection which delivers 3 mL of a solution of icatibant 30 mg.[1,2] Cartons contain one single-use, prefilled syringe.

## 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.[3] On-demand treatment of attacks is most effective when administered early after attack onset.

The guidelines note that HAE with normal C1-INH (HAE-nC1INH) is challenging to diagnose due to the lack of validated biochemical test.[3] Genetic testing could be helpful in confirming diagnosis. The most common mutation linked to HAE-nC1INH is in the F12 gene. These guidelines note the following criteria for diagnosis of HAE-nC1INH: a history of recurrent angioedema without hives and no concomitant use of medication-related angioedema; documented normal or near normal C4, C1-INH antigen, and C1-INH function; and either a mutation associated with the disease or a positive family history of recurrent angioedema and documented lack of efficacy of high-dose antihistamine therapy (i.e., cetirizine at 40 mg/day or the equivalent) for at least 1 month or an interval expected to be associated with three or more angioedema attacks, whichever is longer. With regards to on-demand treatment of HAE-nC1INH, the guidelines note the lack of randomized controlled studies. However, it notes that there are numerous open-label reports with successful responses to on-demand treatments used for HAE type I/II. There are no data on short-term prophylaxis for HAE-nC1INH. Use of C1INH replacement for long-term prophylaxis is noted to be complex and controversial.

An international consensus paper on HAE-nC1INH highlights the lack of high-level evidence, with recommendations based primarily on expert opinion.[4] Six gene mutations (F12, PLG, ANGPT1, KNG1, MYOF, HS3OST6) and two recently identified genes (CPN, DAB2IP) are associated with HAE-nC1INH, though many patients lack a known pathogenic variant. Diagnosis relies on excluding other causes and recognizing features such as recurrent angioedema unresponsive to standard allergy treatments; attacks are typically slower, longer, and more severe than mast-cell mediated angioedema. Effective treatments for acute attacks include plasma-derived C1 INH, icatibant, and ecallantide, while data on prophylaxis are limited, though antifibrinolytics like tranexamic acid may help certain subtypes. Family history supports diagnosis but should not be an absolute criterion due to variability and reliability concerns.

## POLICY STATEMENT

This Drug Quantity Management program has been developed to promote the safe, effective, and economic use of icatibant. 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. All approvals are provided for the duration noted 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 |
|---|---|---|---|
| Firazyr® (icatibant SC injection, generic) | 30 mg/3 mL prefilled syringes | 12 syringes* | 36 syringes* |
| Sajazir™ (icatibant SC injection) | 30 mg/3 mL prefilled syringes | 12 syringes* | 36 syringes* |

SC – Subcutaneous; * This is a quantity sufficient to treat at least four acute hereditary angioedema attacks in each 28-day period (retail) or 12 attacks in an 84-day period (home delivery), assuming that the patient requires three doses in a 24-hour period to treat each attack. If a patient requires additional icatibant doses for a subsequent attack, exceptions are provided based on the criteria below.

**Exceptions to the quantity limits listed above are covered as medically necessary when the following criteria are met. Any other exception is considered not medically necessary.**

### CRITERIA

**1.** If the patient requires additional doses of icatibant to treat a subsequent attack of hereditary angioedema, approve a one-time override for the requested quantity, not to exceed 12 additional prefilled syringes at retail or home delivery.
Note: At retail, the approval quantity should be the number of prefilled syringes of icatibant the patient has received in the past 28 days plus 12 prefilled syringes. At home delivery, the approval quantity should be the number of prefilled syringes of icatibant the patient has received in the past 84 days plus 12 prefilled syringes. ONE override may be approved ONCE every 30 days.

### REFERENCES


1. Firazyr® subcutaneous injection [prescribing information]. Lexington, MA: Takeda; January 2024.
2. Sajazir™ subcutaneous injection [prescribing information]. Cambridge, UK: Cycle; February 2024.
3. 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.
4. Zuraw BL, Bork K, Bouillet L, et al. Hereditary angioedema with normal C1 inhibitor: an updated international consensus paper on diagnosis, pathophysiology, and treatment. *Clin Rev Allergy Immunol.* 2025;68:24.

## HISTORY

| Type of Revision | Summary of Changes | Review Date |
|---|---|---|
| Annual Revision | No criteria changes. | 02/08/2024 |
| Annual Revision | Policy statement was updated to note that "one-time" approvals are provided for 30 days in duration.<br><br>**Icatibant SC injection:** Override criteria were updated to approve a one-time override for 12 additional prefilled syringes if the patient requires additional doses of icatibant to treat a subsequent attack of hereditary angioedema. Previously, criteria approved 3 additional prefilled syringes. Criteria Note was updated to clarify "At retail, the approval quantity should be the number of prefilled syringes of icatibant the patient has received in the past 28 days plus 12 prefilled syringes. At home delivery, the approval quantity should be the number of prefilled syringes of icatibant the patient has received in the past 84 days plus 12 prefilled syringes. ONE override may be approved ONCE every 30 days." | 02/19/2025 |
| Annual Revision | No criteria changes | 02/02/2026 |