

**Clinical Policy: Icatibant (Firazyr)**

Reference Number: CP.PHAR.178

Effective Date: 03.01.16

Last Review Date: 02.21

Line of Business: Commercial, HIM, Medicaid

[Coding Implications](#)[Revision Log](#)

See [Important Reminder](#) at the end of this policy for important regulatory and legal information.

**Description**

Icatibant (Firazyr<sup>®</sup>) is a bradykinin B2 receptor antagonist.

**FDA Approved Indication(s)**

Firazyr is indicated for treatment of acute attacks of hereditary angioedema (HAE) in adults 18 years of age and older.

**Policy/Criteria**

*Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.*

It is the policy of health plans affiliated with Centene Corporation<sup>®</sup> that Firazyr is **medically necessary** when the following criteria are met:

**I. Initial Approval Criteria****A. Hereditary Angioedema** (must meet all):

1. Diagnosis of HAE confirmed by one of the following (a or b):
  - a. Low C4 level and low C1-INH antigenic or functional level (*see Appendix D*);
  - b. Normal C4 level and normal C1-INH levels, and both of the following (i and ii):
    - i. History of recurrent angioedema;
    - ii. Family history of angioedema;
2. Prescribed by or in consultation with a hematologist, allergist, or immunologist;
3. Age ≥ 18 years;
4. Prescribed for treatment of acute HAE attacks;
5. Generic version of Firazyr is prescribed, unless medical justification supports inability to use the generic (e.g., contraindications to excipients in the generic);
6. Member is not using Firazyr in combination with another FDA-approved product for treatment of acute HAE attacks (e.g., Berinert<sup>®</sup>, Ruconest<sup>®</sup>, Kalbitor<sup>®</sup>);
7. Dose does not exceed 30 mg (1 syringe) per dose, with up to 3 doses administered in a 24-hour period.

**Approval duration: Up to 6 doses per month**

**Medicaid/HIM** – 6 months

**Commercial** – 6 months or to the member's renewal date, whichever is longer

**B. Other diagnoses/indications**

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is

NOT authorized): CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

## II. Continued Therapy

### A. Hereditary Angioedema (must meet all):

1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
2. Member is responding positively to therapy;
3. Member is not using Firazyr in combination with another FDA-approved product for treatment of acute HAE attacks (e.g., Berinert, Ruconest, Kalbitor);
4. If request is for a dose increase, new dose does not exceed 30 mg (1 syringe) per dose, with up to 3 doses administered in a 24-hour period.

**Approval duration: Up to 6 doses per month**

**Medicaid/HIM** – 12 months

**Commercial** – 6 months or to the member's renewal date, whichever is longer

### B. Other diagnoses/indications (must meet 1 or 2):

1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.

**Approval duration: Duration of request or 6 months (whichever is less); or**

2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

## III. Diagnoses/Indications for which coverage is NOT authorized:

- A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid or evidence of coverage documents.

## IV. Appendices/General Information

### *Appendix A: Abbreviation/Acronym Key*

CI-INH: C1 esterase inhibitor

C4: complement component 4

FDA: Food and Drug Administration

HAE: hereditary angioedema

### *Appendix B: Therapeutic Alternatives*

Not applicable

### *Appendix C: Contraindications/Boxed Warnings*

None reported

### *Appendix D: General Information*

- Diagnosis of HAE:
  - There are two classifications of HAE: HAE with C1-INH deficiency (further broken down into Type 1 and Type II) and HAE of unknown origin (also known as Type III).

- In both Type I (~85% of cases) and Type II (~15% of cases), C4 levels are low. C1-INH antigenic levels are low in Type I while C1-INH functional levels are low in Type II. Diagnosis of Type I and II can be confirmed with laboratory tests. Reference ranges for C4 and C1-INH levels can vary across laboratories (see below for examples); low values confirming diagnosis are those which are below the lower end of normal.

Laboratory Test & Reference Range	Mayo Clinic	Quest Diagnostics	LabCorp
C4	14-40 mg/dL	16-47 mg/dL	13-44 mg/dL
C1-INH, antigenic	19-37 mg/dL	21-39 mg/dL	21-39 mg/dL
C1-INH, functional	Normal: > 67% Equivocal: 41-67% Abnormal: < 41%	Normal: ≥ 68% Equivocal: 41-67% Abnormal: ≤ 40%	Normal: > 67% Equivocal: 41-67% Abnormal: < 41%

- Type III, on the other hand, presents with normal C4 and C1-INH levels. Some patients have an associated mutation in the FXII gene, while others have no identified genetic indicators. Type III is very rare (number of cases unknown), and there are no laboratory tests to confirm the diagnosis. Instead, the diagnosis is clinical and supported by recurrent episodes of angioedema with a strong family history of angioedema.

## V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Treatment of acute HAE attacks	30 mg SC in the abdominal area; if response is inadequate or symptoms recur, additional injections of 30 mg may be administered at intervals of at least 6 hours.  Do not administer more than 3 injections in 24 hours.	90 mg/24 hours

## VI. Product Availability

Single-use prefilled syringe: 30 mg/3 mL

## VII. References

1. Firazyr Prescribing Information. Lexington, MA: Shire Orphan Therapies, Inc.; August 2020. Available at: [www.firazyr.com](http://www.firazyr.com). Accessed October 2, 2020.
2. Cicardi M, Bork K, Caballero T, et al. Evidence-based recommendations for the therapeutic management of angioedema owing to hereditary C1 inhibitor deficiency: consensus report of an International Working Group. *Allergy*. 2012; 67(2): 147-157.
3. Cicardi M, Aberer W, Banerji A, et al. Classification, diagnosis, and approach to treatment for angioedema: consensus report from the Hereditary Angioedema International Working Group. *Allergy*. 2014; 69(5): 602-616.
4. Craig T, Pursun E, Bork K, et al. WAO guideline for the management of hereditary angioedema. *WAO Journal*. 2012; 5: 182-199.
5. Zuraw BL, Banerji A, Bernstein JA, et al. US Hereditary Association Medical Advisory Board 2013 recommendations for the management of hereditary angioedema due to C1 inhibitor deficiency. *J Allergy Clin Immunol*. 2013; 1(5): 458-467.

6. Zuraw BL, Bernstein JA, Lang DM, et al. A focused parameter update: hereditary angioedema, acquired C1 inhibitor deficiency, and angiotensin-converting enzyme inhibitor-associated angioedema. *J Allergy Clin Immunol.* 2013; 131(6): 1491-1493.
7. Maurer M, Magerl M, Ansotegui I, et al. The international WAO/EAACI guideline for the management of hereditary angioedema – the 2017 revision and update. *Allergy.* 2018; 73(8):1575-1596.
8. Mayo Clinic Laboratories [internet database]. Rochester, Minnesota: Mayo Foundation for Medical Education and Research. Updated periodically. Accessed November 4, 2019.
9. Quest Diagnostics ® [internet database]. Updated periodically. Accessed November 4, 2019.
10. LabCorp [internet database]. Burlington, North Carolina: Laboratory Corporation of America. Updated periodically. Accessed November 4, 2019.

### Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J1744	Injection, icatibant, 1 mg

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Medicaid: Added criteria to confirm diagnosis. Removed age requirement. Increased approval duration to 12 months and added recommended dosing. Added criteria for continued approval.	03.17	03.17
1Q18 annual review: Policies combined for medicaid, HIM and commercial lines of business; No significant change from previously approved corporate policy; HIM/Medicaid: added specialist requirement, removed “Other types of angioedema have been ruled out” from part of diagnosis due to its subjective nature, while specialist has been added; Added age limit; References reviewed and updated	11.15.17	02.18
1Q 2019 annual review: added quantity limit of 6 doses per month for treatment of acute attacks; for Commercial, revised approval duration to 6 months or member’s renewal date; removed approval duration for HNCA/HNMC as it does not apply to this policy; added requirement that member is not using requested product in combination with other approved treatments for the treatment of acute HAE attacks; references reviewed and updated.	10.30.18	02.19
1Q 2020 annual review: HAE lab reference range updated; initial auth duration revised to 6 months for alignment; references reviewed and updated.	11.04.19	02.20

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Added requirement for generic Firazyr use for all indications.	03.31.20	
1Q 2021 annual review: no significant changes; references to HIM.PHAR.21 revised to HIM.PA.154; references reviewed and updated.	10.02.20	02.21

### **Important Reminder**

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. “Health Plan” means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan’s affiliates, as applicable.

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**Note:**

**For Medicaid members,** when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

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