Clinical Policy: Icatibant (Firazyr)

Reference Number: PA.CP.PHAR.178
Effective Date: 01/18
Last Review Date: 07/18

Coding Implications
Revision Log

Description
The intent of the criteria is to ensure that patients follow selection elements established by Pennsylvania Health and Wellness® clinical policy for icatibant (Firazyr®).

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
It is the policy of Pennsylvania Health and Wellness® that Firazyr is **medically necessary** when one of the following criteria is met:

I. Initial Approval Criteria

A. Hereditary Angioedema (HAE) (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 B);
   b. Normal C4 level and normal C1-INH levels, and all of the following (i - 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. Dose does not exceed 30 mg per dose (1 syringe per dose) with up to 3 doses administered in a 24-hour period.

Approval duration: 12 months

B. Other diagnoses/indications: Refer to PA.CP.PMN.53

II. Continued Approval

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

1. Currently receiving medication via Pennsylvania Health and Wellness benefit or member has previously met initial approval criteria or the Continuity of Care policy (PA.LTSS.Phar.01) applies ;
2. Documentation of positive response to therapy;
3. Prescribed dose does not exceed 30 mg per dose (1 syringe per dose) with up to 3 doses administered in a 24 hour period.

Approval duration: 12 months

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

1. Currently receiving medication via Pennsylvania Health and Wellnesss benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.LTSS.PHAR.01) applies; or
2. Refer to PA.CP.PMN.53

Background

Description/Mechanism of Action:

Firazyr (icatibant) is a competitive antagonist selective for the bradykinin B2 receptor, with an affinity similar to bradykinin. HAE is caused by an absence or dysfunction of C1-INH, a key regulator of the Factor XII/kallikrein proteolytic cascade that leads to bradykinin production. Bradykinin is a vasodilator which is thought to be responsible for the characteristic HAE symptoms of localized swelling, inflammation, and pain. Icatibant inhibits bradykinin from binding the B2 receptor and thereby treats the clinical symptoms of an acute, episodic attack of HAE.

Formulations:

Firazyr is supplied as a single-use, prefilled syringe for subcutaneous administration which delivers 3 mL of a sterile solution of icatibant 30 mg.

Appendices

Appendix A: Abbreviation Key

ACE-I: angiotensin-converting enzyme inhibitor
ARB: angiotensin receptor blocker
CI-INH: C1 esterase inhibitor
HAE: hereditary angioedema

Appendix B: 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 1 (~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	9-36 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.

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	Approval Date
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	02/18	

References
1. Firazyr Prescribing Information. Lexington, MA: Shire Orphan Therapies, Inc.; December 2015. Available at: www.firazyr.com. Accessed November 15, 2017.
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.