Cigna National Preferred Formulary Coverage Policy

Effective Date 1/1/2021
Next Review Date… 1/1/2022
Coverage Policy Number NPF404

Prior Authorization
Hereditary Angioedema - Icatibant (Firazyr®) (injection for subcutaneous use)

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Related Coverage Resources

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. 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.

NPF Coverage Policy

Cigna covers icatibant (Firazyr®) as medically necessary when the following criteria are met for FDA Indications or Other Uses with Supportive Evidence:

Prior authorization is recommended for prescription benefit coverage of icatibant. Because of the specialized skills required for evaluation and diagnosis of individuals treated with icatibant, approval requires it to be prescribed by or in consultation with a physician who specializes in the condition being treated. All approvals are provided for the duration noted below.

Documentation: Documentation will be required where noted in the criteria as **[documentation required]**. Documentation may include, but is not limited to, chart notes, laboratory records, and prescription claims records.

FDA Indication(s)

1. **Hereditary Angioedema (HAE) Due to C1 Inhibitor (C1-INH) Deficiency (Type I or Type II) – Treatment of Acute Attacks.** Approve for the duration noted if the individual meets one of the following criteria (A or B):
   - **A)** Initial therapy. Approve for 1 year if the individual meets both of the following criteria (i and ii):
     - **i.** Individual has HAE type I or type II as confirmed by the following diagnostic criteria (a and b):
       - **a)** Individual has low levels of functional C1-INH protein (< 50% of normal) at baseline, as defined by the laboratory reference values **[documentation required]**; AND
       - **b)** Individual has lower than normal serum C4 levels at baseline, as defined by the laboratory reference values **[documentation required]**; AND
     - **ii.** The medication is prescribed by, or in consultation with, an allergist/immunologist or a physician who specializes in the treatment of HAE or related disorders.
   - **B)** Individual who has treated previous acute HAE attacks with icatibant (Firazyr). Approve for 1 year if the individual meets all of the following criteria (i, ii, and iii):
     - **i.** Individual has a diagnosis of HAE type I or type II **[documentation required]**; AND
     - **ii.** According to the prescriber, the individual has had a favorable clinical response (e.g., decrease in the duration of HAE attacks, quick onset of symptom relief, complete resolution of symptoms, decrease in HAE acute attack frequency or severity) with icatibant treatment; AND
     - **iii.** The medication is prescribed by or in consultation with an allergist/immunologist or a physician who specializes in the treatment of HAE or related disorders.

Conditions Not Covered

Icatibant (Firazyr®) is considered experimental, investigational or unproven for ANY other use including the following (this list may not be all inclusive):

1. **Hereditary Angioedema (HAE) Prophylaxis**. Data are not available and icatibant is not indicated for prophylaxis of HAE attacks.

Background

Overview
Icatibant (Firazyr, generics) is a synthetic decapeptide that is indicated for the treatment of acute hereditary angioedema (HAE) attacks in adults ≥ 18 years of age.[1] Icatibant is a competitive bradykinin B2 receptor antagonist with an affinity similar to bradykinin. Bradykinin is a vasodilator which is likely responsible for the characteristic HAE symptoms of localized swelling, inflammation and pain. By preventing the binding of bradykinin to its receptor, icatibant treats the clinical symptoms of an acute HAE attack.

Disease Overview
HAE due to C1 esterase inhibitor (C1-INH) deficiency has two subtypes: HAE type I and HAE type II. HAE diagnosis can be confirmed by measuring functional C1-INH protein levels (usually < 50% of normal in individuals with HAE), C4 levels, and C1-INH antigenic levels.[2,3] Individuals with HAE type I have low C4 and C1-INH antigenic protein levels, along with low levels of functional C1-INH protein. Individuals with HAE type II have low C4 and functional C1-INH protein level, with a normal or elevated C1-INH antigenic protein level. C1-INH replacement therapies are appropriate for both HAE type I and type II.

Individuals with the third type of HAE called HAE with normal C1-INH (HAE nC1-INH), previously referred to as HAE type III, have normal C4 and C1-INH antigenic protein levels.[2] HAE is much less prevalent than HAE types I/II, and the exact cause of HAE nC1-INH has not been determined.[2,4] Pathogenic variants in the genes encoding for Factor XII (regulates bradykinin generation), angiopoietin-1 (involved in vascular permeability), and plasminogen have been associated with HAE nC1-INH; however, the majority of cases have unknown etiology. There are no randomized or controlled clinical trial data available with any therapy for use in HAE nC1-INH.[4-6]

Guidelines
Per the World Allergy Organization/European Academy of Allergy and Clinical Immunology guidelines (2017), all HAE type I/II attacks should be considered for acute treatment; treatment is mandatory for any attack potentially affecting the upper airway (HAE nC1-INH is not addressed within the scope of the guideline).[3] Attacks should be treated as early as possible. Self-administration at home facilitates earlier response. The guidelines recommend C1-INH products, Kalbitor® (ecallantide for subcutaneous injection), or icatibant as first-line treatment options. Androgens and antifibrinolytics are not effective as acute treatment. Individuals should carry acute treatment with them at all times and should have enough supply on hand for treatment of two attacks. Other guidelines from the US Hereditary Angioedema Association Medical Advisory Board (2013), a practice parameter update from a Joint Task Force (2013), and an international and Canadian guideline (2019) have similar recommendations regarding acute treatment of HAE type I/II attacks.[4,7,8]

References

1. Firazyr® [prescribing information]. Lexington, MA: Shire/Takeda; April 2020.
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3. Mauer 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. Available at: https://onlinelibrary.wiley.com/doi/epdf/10.1111/all.13384. Accessed on August 11, 2020.
4. Betschel S, Badiou J, Binkley K, et al. The International/Canadian Hereditary Angioedema Guideline [published correction appears in Allergy Asthma Clin Immunol. 2020 May 6;16:33]. *Allergy Asthma Clin Immunol*. 2019;15:72. Available at: https://aacijournal.biomedcentral.com/articles/10.1186/s13223-019-0376-8. Accessed on August 4, 2020.
5. Zuraw BL, Bork K, Binkley KE, et al. Hereditary angioedema with normal C1 inhibitor function: consensus of an international expert panel. *Allergy Asthma Proc.* 2012;33:S145-S156.
6. Magerl M, Germenis AE, Maas C, et al. Hereditary angioedema with normal C1 inhibitor. Update on evaluation and treatment. *Immunol Allergy Clin N Am.* 2017;37:571-584.
7. Zuraw BL, Banerji A, Bernstein JA, et al. US Hereditary Angioedema Association Medical Advisory Board 2013 recommendations for the management of hereditary angioedema due to C1 inhibitor deficiency. *J Allergy Clin Immunol: In Practice*. 2013;1:458-467. Available at: https://haei.org/wp-content/uploads/2015/04/Zuraw-B-L-US-HAEA-MAB-2013-Recommendations.pdf. Accessed on August 11, 2020.
8. Zuraw BL, Bernstein JA, Lang DM. 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.e25.

Last Revision Details

Annual revision	"Prescribing physician" updated to "prescriber" throughout criteria.	08/19/2020