PRIOR AUTHORIZATION POLICY

POLICY: Hereditary Angioedema – Icatibant (Firazyr) Prior Authorization Policy
- Firazyr® (icatibant injection for subcutaneous use – Shire/Takeda)
- Icatibant injection for subcutaneous use – various

REVIEW DATE: 08/19/2020

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 patients with HAE), C4 levels, and C1-INH antigenic levels.[2,3] Patients with HAE type I have low C4 and C1-INH antigenic protein levels, along with low levels of functional C1-INH protein. Patients 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.

Patients 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. Patients 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]

POLICY STATEMENT

Prior authorization is recommended for prescription benefit coverage of icatibant. Because of the specialized skills required for evaluation and diagnosis of patients 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.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of icatibant is recommended in those who meet the following criteria:

FDA-Approved Indications

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 patient meets one of the following criteria (A or B):
   - **A)** Initial therapy. Approve for 1 year if the patient meets both of the following criteria (i and ii):
     - **i.** Patient has HAE type I or type II as confirmed by the following diagnostic criteria (a and b):
       - **a)** Patient has low levels of functional C1-INH protein (< 50% of normal) at baseline, as defined by the laboratory reference values **[documentation required]**; AND
       - **b)** Patient 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)** Patient who has treated previous acute HAE attacks with icatibant (Firazyr). Approve for 1 year if the patient meets all of the following criteria (i, ii, and iii):
     - **i.** Patient has a diagnosis of HAE type I or type II **[documentation required]**; AND
     - **ii.** According to the prescriber, the patient 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 RECOMMENDED FOR APPROVAL

Coverage of icatibant is not recommended in the following circumstances:

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

2. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

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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.
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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.