Prior approval is required for some or all procedure codes listed in this Corporate Drug Policy.

**OVERVIEW**

Firazyr is a bradykinin B2 receptor antagonist indicated for treatment of acute attacks of hereditary angioedema (HAE) in adults 18 years of age or older. Bradykinin is a vasodilator which is likely responsible for the characteristic HAE symptoms of localized swelling, inflammation and pain. Firazyr competitively inhibits the binding of bradykinin to the B2 receptor, which reduces the effects of bradykinin thereby treating the symptoms associated with HAE. The safety and efficacy of Firazyr for prophylactic therapy has not been established.

Hereditary angioedema is a rare, debilitating, potentially life-threatening genetic disorder caused by a deficiency in C1-INH, a plasma protein involved in the regulation of the complement and intrinsic coagulation pathways. Hereditary angioedema is caused by mutations in the C1-INH gene located on chromosome 11q and inherited as an autosomal dominant trait. Two main types of hereditary angioedema exist: mutations causing Type I hereditary angioedema are associated with decreased production of C1-INH leading to decreased functional levels; Type II hereditary angioedema mutations are associated with a dysfunctional C1 inhibitor, but the inhibitor level is normal.

HAE is characterized by recurrent episodes of nonpruritic, nonpitting, subcutaneous or submucosal edema associated with pain syndrome, nausea, vomiting, diarrhea, and/or life-threatening airway swelling. Airway obstruction due to swelling is life-threatening if left untreated. There is a wide variation in the frequency and severity of attacks. Clinical experience suggests that minor trauma and/or stress, among other triggers, may precipitate attacks. Untreated attacks typically last over 48 to 96 hours. Short-term prophylaxis with a C1-INH - is recommended if more than minor manipulation (e.g., mild dental work) is needed, and prior to intubation or major procedures. The dose for short-term prophylaxis with C1-INH varies from 10 U/kg to 20 U/kg or 1000 units, 1 to 6 hours before procedure. Long-term prophylaxis should be considered in all severely symptomatic patients, taking into consideration the severity of disease, frequency of attacks, patient’s quality of life, availability of resources, and failure to achieve adequate control by on-demand therapy.

**POLICY STATEMENT**

This policy involves the use of Firazyr. Prior authorization is recommended for pharmacy and medical benefit coverage of Firazyr. Approval is recommended for those who meet the conditions of coverage in the Criteria, Dosing, Initial/Extended Approval, Duration of Therapy, and Labs/Diagnostics for the diagnosis provided. Waste Management applies for all...

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<tr>
<th>Policy:</th>
<th>201509</th>
<th>Initial Effective Date: 04/21/2016</th>
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<tbody>
<tr>
<td>Code(s):</td>
<td>HCPCS J1744</td>
<td>Annual Review Date: 03/21/2019</td>
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<tr>
<td>SUBJECT:</td>
<td>Firazyr (icatibant injection for subcutaneous use)</td>
<td>Last Revised Date: 08/15/2019</td>
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covered conditions that are administered by a healthcare professional. **Conditions Not Recommended for Approval** are listed following the recommended authorization criteria and Waste Management section. Requests for uses not listed in this policy will be reviewed for evidence of efficacy and for medical necessity on a case-by-case basis.

Because of the specialized skills required for evaluation and diagnosis of patients treated with Firazyr as well as the monitoring required for AEs and long-term efficacy, initial approval requires Firazyr be prescribed by or in consultation with a physician who specializes in the condition being treated. All approvals for initial therapy are provided for the initial approval duration noted below; if reauthorization is allowed, a response to therapy is required for continuation of therapy unless otherwise noted below.

**RECOMMENDED AUTHORIZATION CRITERIA**
Coverage of Firazyr is recommended in those who meet the following criteria:

**Food and Drug Administration (FDA)-Approved Indications**

1. **Initial - Acute Attacks of Hereditary Angioedema (HAE), Type 1 or Type 2.** Approve Firazyr if ALL of the following are met (a, b, c, d, e, f AND g):

   a) The patient has HAE as confirmed by the following diagnostic criteria (i OR ii) [documentation required]:

      i) Patient has low levels of functional C1-INH protein (below 67% or as defined by the laboratory reference values); OR
      ii) Patient has lower than normal serum C4 levels (< 14 mg/dL or as defined by the laboratory reference values) AND lower than normal C1-INH level (< 19.9 mg/dL or as defined by the laboratory reference values); AND

   b) Prescribed by, or in consultation with, an allergist/immunologist or a physician that specializes in the treatment of HAE or related disorders; AND

   c) Patient is 18 years of age or older; AND

   d) Patient has at least ONE of the following criteria (i, ii, OR iii)

      i. Patient must have history of self-limiting, non-inflammatory subcutaneous angioedema, without urticaria, which is recurrent and lasts >12 hours
      ii. Self-limiting, recurrent abdominal pain without a clear organic cause lasting >6 hours
      iii. A history of laryngeal edema; AND

   e) All other causes of acquired angioedema (for example, medications, autoimmune diseases) have been excluded; AND

   f) Firazyr is not used in combination with other approved treatments for acute HAE attacks (e.g. Berinert, Kalbitor, or Ruconest).
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2. **Patient has been started on Firazyr for Acute Attacks of Hereditary Angioedema (HAE), Type 1 or Type 2.**
   Approve for continuation of therapy if **ALL** of the following are met (a, b, c, d, e, f, g **AND** h):

   a) The patient has HAE as confirmed by the following diagnostic criteria (i **OR** ii) **[documentation required]**:
      i) Patient has low levels of functional C1-INH protein (below 67% or as defined by the laboratory reference values); OR
      ii) Patient has lower than normal serum C4 levels (< 14 mg/dL or as defined by the laboratory reference values) 
         AND lower than normal C1-INH level (< 19.9 mg/dL or as defined by the laboratory reference values); AND

   b) Prescribed by, or in consultation with, an allergist/immunologist or a physician that specializes in the treatment of 
      HAE or related disorders; AND

   c) Patient is 18 years of age or older; AND

   d) Patient has at least ONE of the following criteria (i, ii, **OR** iii)
      i. Patient must have history of self-limiting, non-inflammatory subcutaneous angioedema, without urticaria, which is recurrent and lasts >12 hours
      ii. Self-limiting, recurrent abdominal pain without a clear organic cause lasting >6 hours
      iii. A history of laryngeal edema; AND

   e) All other causes of acquired angioedema (for example, medications, autoimmune diseases) have been excluded; AND

   f) Firazyr is not used in combination with other approved treatments for acute HAE attacks (e.g. Berinert, Kalbitor, 
      or Ruconest).

   g) Patient has at least 1 annual assessment by an HAE specialist.

   h) If the requested medication is brand Firazyr, the patient has failed on or has an intolerance to the generic, icatibant 
      for at least 3 months.

**Initial Approval/ Extended Approval.**

A) **Initial Approval:** 365 days (1 year)
B) **Extended Approval:** 365 days (1 year)

**MMO Site of Care Medical Necessity Criteria:**

- Medications in this policy will be administered in a place of service that identifies the location to be a non-
  hospital facility based location (i.e., home infusion provider, provider’s office, free-standing ambulatory infusion 
  center) unless **at least one** of the following are met:

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1. Age less than 21 years; or
2. Clinically unstable based upon documented medical history (e.g., patient is hemodynamically unstable); or
3. History of a severe adverse event from previous administration of the prescribed medication; or
4. Requested medication is being administered as follows:
   ▪ part of a chemotherapy regimen (e.g., anti-neoplastic agent, colony stimulating factor, erythropoiesis-stimulating agent, anti-emetic) for treatment of cancer; or
   ▪ administered with dialysis; or
5. Physical or cognitive impairment and caregiver is not available to assist with safe administration of prescribed medication in the home; or
6. Up to 1 dose of medication or re-initiation after at least 12 months; or
7. Experiencing adverse events that are not managed by premedication or resources available at a non-hospital facility-based location.

†This criterion does not apply to Medicare or Medicare Advantage members.

Prior approval is required for HCPCS Code J1744.

Documentation Requirements:

The Company reserves the right to request additional documentation as part of its coverage determination process. The Company may deny reimbursement when it has determined that the drug provided or services performed were not medically necessary, investigational or experimental, not within the scope of benefits afforded to the member and/or a pattern of billing or other practice has been found to be either inappropriate or excessive. Additional documentation supporting medical necessity for the services provided must be made available upon request to the Company. Documentation requested may include patient records, test results and/or credentials of the provider ordering or performing a service. The Company also reserves the right to modify, revise, change, apply and interpret this policy at its sole discretion, and the exercise of this discretion shall be final and binding.

REFERENCES

- Firazyr® [prescribing information]. Lexington, MA: Shire Orphan Therapies Inc; December 2015.

| HCPCS Code(s): | J1744 Injection, icatibant 1 mg |