Clinical Policy Title:	icatibant
Policy Number:	RxA.136
Drug(s) Applied:	Firazyr®
Original Policy Date:	02/07/2020
Last Review Date:	03/09/2021
Line of Business Policy Applies to:	All lines of business

Background

Icatibant (Firazyr®) is a bradykinin B2 receptor antagonist. It is indicated for treatment of acute attacks of hereditary angioedema (HAE) in adults 18 years of age and older.

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
icatibant (Firazyr®)	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 within 24-hour period. Patients may self-administer upon recognition of an HAE attack.	90 mg/24 hours

Dosage Forms

- Injection: 10 mg per mL

Clinical Policy

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

I. Initial Approval Criteria

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

1. Documented diagnosis of type I or II HAE confirmed by one of the following (a or b):
   a. Low C4 level, low C1-INH antigenic or functional levels (*see Appendix D*), and history of recurrent angioedema;

   b. Normal C4 level, normal C1-INH antigenic and functional levels, and both of the following (i and ii):
      i. History of recurrent angioedema;
      ii. Family history of angioedema OR demonstration of mutation associated with disease;
2. Prescribed by or in consultation with an hematologist, allergist, pulmonologist or immunologist;
3. Age ≥ 18 years;
4. Prescribed for treatment of acute HAE attacks;
5. Member has had at least 1 severe attack within the past 6 months;
6. Member is not using icatibant in combination with another FDA-approved product for treatment of acute HAE attacks (e.g., Berinert®, Ruconest®, Kalbitor®); and
7. Dose does not exceed 30 mg (1 syringe) per dose, with up to 3 doses administered within a 24-hour period.

Approval duration
Commercial: 12 months
Medicaid: 12 months

II. Continued Therapy Approval

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

1. Currently receiving medication that has been authorized by RxAdvance or member has previously met initial approval criteria listed in this policy;
2. Member is experiencing improvement in symptoms of acute HAE attacks;
3. Member is not using icatibant 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 within a 24-hour period.

Approval duration
Commercial: 12 months
Medicaid: 12 months

III. Appendices

APPENDIX A: Abbreviation/Acronym Key
C4: complement 4
C1-INH: C1 esterase inhibitor
FDA: Food and Drug Administration
HAE: hereditary angioedema
SC: subcutaneous

APPENDIX B: Therapeutic Alternatives
Not applicable.

APPENDIX C: Contraindications/Boxed Warnings

- Contraindication(s):
  - None reported.

- Boxed Warning(s):
  - 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 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.

References

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Review/Revision History	Review/Revision Date	P&T Approval Date
Policy established.	01/2020	02/07/2020
Policy reviewed & updated.	04/28/2020	05/20/2020
Policy was reviewed. 1. Policy title table was updated. 2. Dosage form section was updated. 3. Initial approval criteria I.A.1 was updated based on updated guidelines. 4. Approval duration for commercial plans was updated for initial and continued approval criteria. 5. Continued therapy criteria II.A.1 was rephrased to "Currently receiving medication that has been authorized by RxAdvance..." 6. Appendix A updated to add C4. 7. References reviewed and updated.	01/25/2021	03/09/2021