Title: **Acute Attacks of Hereditary Angioedema (HAE): C1 esterase inhibitor (Berinert), icatibant (Firazyr®), ecallantide (Kalbitor®), C1 esterase inhibitor recombinant (Ruconest®)**

| Approval: Robert Bonnell, M.D., Med. Dir. | DATES - Origination: 02/12/12 |
| Responsible Party: CPM Director | Revised: 02/28/14 | Effective: 06/16/14 |
| Distribution: Medical Department | P&T Review: 08/24/16 | Annual Review: 08/24/16 |

**Purpose:**

To provide guidelines and criteria for the review and decision determination of requests for medications that requires prior authorization.

**Implementation Information:**

1.0 Under the supervision of the Clinical Pharmacy Management (CPM) Director, the CPM staff is responsible for the development of guidelines and criteria for use by the Medical Department.

2.0 Staff utilizing this procedure is monitored via individual departmental audit tools.

3.0 Medical Department staff has access to the *Medical Department Procedure Manual* and receives notice from management when procedures are developed, revised, or archived:

3.1 On an annual basis or more often when indicated, the Medical Department Procedures are reviewed by medical staff for the purpose of developing, revising, or archiving.

**Background Information:**

**Reference Statement**

- Guidelines are compiled from available US Food and Drug Administration (FDA) approved indications, general practice guidelines, and/or evidence-based uses established through phase III clinical studies without published conflicting data. Only clinical studies published in their entirety in reputable peer-reviewed journals will be evaluated.
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**Background Information, continued:**

**Medication Summary**

- **C1 esterase inhibitor (Berinert)** is an FDA approved medication used to treat acute abdominal, facial, or laryngeal attacks of HAE in those 12 years and older. Berinert is administered as a slow IV injection upon recognition of an HAE attack.
- **Icatibant (Firazyr®)** is a selective bradykinin B2 receptor antagonist used subcutaneously to treat acute attacks of hereditary angioedema (HAE) in adults. Icatibant is administered upon recognition of an acute HAE attack. If symptoms persist or relapse after at least six (6) hours following the initial icatibant dose, additional doses may be administered (up to 3 doses in 24 hours).
- **Ecallantide (Kalbitor®)** is a kallikrein inhibitor used subcutaneously to treat acute hereditary angioedema (HAE) attacks in those 12 years and older. Ecallantide is administered upon recognition of an acute HAE attack. If the symptoms persist, an additional dose may be administered within a 24 hour period.
- **C1 esterase inhibitor, recombinant (Ruconest®)** is an FDA approved medication used to treat acute angioedema attacks in adolescents and adults with HAE. This medication is an analog of human C1 esterase inhibitor obtained from the milk of rabbits. Effectiveness of Ruconest® has not been established in patients with laryngeal attacks. Ruconest® is administered as a slow IV infusion. If symptoms persist, a second dose can be administered within a 24 hour period.
- **Hereditary angioedema (HAE)** causes subcutaneous and submucosal edema that can affect the upper airways, face, extremities, genitals, and gastrointestinal tract. If an HAE attack involves the larynx or oropharynx, the attack can be life-threatening.
- **Firazyr® and Ruconest®** may be self-administered after proper training by a healthcare professional. Berinert (C1 inhibitor, human) may also be self-administered by Members. Ecallantide should only be administered by a healthcare professional with appropriate medical support to manage anaphylaxis and hereditary angioedema.
- Members experiencing laryngeal symptoms associated with an HAE should seek medical attention immediately in a healthcare facility following administration of any of these medications.
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Coverage Guidelines
- Member must be eligible and have applicable benefit coverage.
- Prior authorization requests that do not meet clinical criteria in this Procedure will be forwarded to a Clinical Pharmacist for review.

Exclusion Criteria
- Member less than 12 years old for Berinert and Kalbitor®; less than 13 years of age for Ruconest®; less than 18 years old for Firazyr®.
- Member has taken an ACE Inhibitor or estrogen replacement therapy within the last month.
- For Ruconest®: Allergy to rabbits or rabbit-derived products (leporine protein hypersensitivity)
- For Ruconest®: Effectiveness not established in HAE patients with laryngeal attacks

Additional Information
- AvMed’s Clinical Pharmacists are licensed by the State of Florida.
- AvMed’s Medical Directors are Board Certified physicians licensed by the State of Florida.

Procedure:

1.0 Request for initial therapy with icatibant (Firazyr®) requires documentation from the Member’s medical records maintained by the requesting independent practitioner’s office verifying the following:

1.1 Member has been diagnosed with hereditary angioedema by an allergist, immunologist or a hematologist; AND

1.2 Member has a documented serum C4 and C1-INH (antigenic or functional) level below the lower limit of normal as defined by the laboratory’s normal reference range; AND

1.3 Member has a history of acute abdominal and/or laryngeal attacks and must be experiencing at least one (1) of the following:
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Procedure, continued:

1.3.1 Airway swelling;
1.3.2 Severe abdominal pain;
1.3.3 Facial swelling;
1.3.4 Painful facial distortion; AND

1.4 Member has a documented intolerance to or treatment failure to Berinert; AND

1.5 Member is having less than four (4) attacks per month;

1.6 Cannot be used concomitantly with either Berinert, Kalbitor®, or Ruconest®; AND

1.7 If criteria are met, Member may receive a maximum of three (3) syringes in any one (1) month for a maximum of three (3) months.

2.0 Request for continuation of therapy with icatibant (Firazyr®) requires documentation from the Member’s medical records maintained by the requesting independent practitioner’s office verifying the following:

2.1 Member had adequate response to previously administered doses of Firazyr®; AND

2.2 All criteria for initial therapy are met;

2.3 If criteria are met, Member may receive a maximum of three (3) syringes in any one (1) month for a maximum of three (3) months.

3.0 Request for initial therapy with ecallantide (Kalbitor®) requires documentation from the Member’s medical records maintained by the requesting independent practitioner’s office verifying the following:
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3.1 Member has been diagnosed with hereditary angioedema by an allergist, immunologist or a hematologist; AND

3.2 Member has a documented serum C4 and C1-INH (antigenic or functional) level below the lower limit of normal as defined by the laboratory’s normal reference range; AND

3.3 Member has a history of acute abdominal and/or laryngeal attacks and must be experiencing at least one (1) of the following:

3.3.1 Airway swelling;
3.3.2 Severe abdominal pain;
3.3.3 Facial swelling;
3.3.4 Painful facial distortion; AND

3.4 Member has a documented intolerance to or treatment failure to Berinert AND Firazyr® (Members aged 12-17 years old only need treatment failure to Berinert); AND

3.4 Member is having less than four (4) attacks per month;

3.5 Cannot be used concomitantly with either Berinert, Firazyr®, or Ruconest®, AND

3.6 If criteria are met, approve a maximum of six (6) vials in any one (1) month for a maximum of three (3) months.

4.0 Request for continuation of therapy with ecallantide (Kalbitor®) requires documentation from the Member’s medical records maintained by the requesting independent practitioner’s office verifying the following:

4.1 Member had adequate response to previously administered doses of Kalbitor®; AND
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4.2 All criteria for initial therapy are met;

4.3 If criteria are met, approve a maximum of six (6) vials in any one (1) month for a maximum of three (3) months.

5 Request for initiation therapy with C1 esterase inhibitor, Recombinant (Ruconest®) requires documentation from the Member’s medical records maintained by the requesting independent practitioner’s office verifying the following:

5.1 Member has been diagnosed with hereditary angioedema by an allergist, immunologist or a hematologist; AND

5.2 Member has a documented serum C4 and C1-INH (antigenic or functional) level below the lower limit of normal as defined by the laboratory’s normal reference range; AND

5.3 Member has a history of acute abdominal or facial attacks and must be experiencing at least one (1) of the following:

5.3.1 Airway swelling;
5.3.2 Severe abdominal pain;
5.3.3 Facial swelling;
5.3.4 Painful facial distortion; AND

5.4 Member has a documented intolerance to or treatment failure of Berinert AND Firazyr® (Members aged 12-17 years old need treatment failure to Berinert); AND

5.5 Member is having less than four (4) attacks per month;

5.6 Cannot be used concomitantly with either Berinert, Kalbitor®, or Firazyr®; AND

5.7 Body weight is provided to follow dosing as directed:
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<table>
<thead>
<tr>
<th>Body Weight</th>
<th>Dose</th>
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<tbody>
<tr>
<td>Less than 84 kg</td>
<td>50 IU/kg IV</td>
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<tr>
<td>84 kg or greater</td>
<td>4200 IU (2 vials) IV</td>
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Procedure, continued:

5.8 If criteria are met, approve for a maximum of six (6) vials in any one (1) month for a maximum of three (3) months.

6. Request for continuation of therapy with C1 esterase inhibitor, Recombinant (Ruconest®) requires documentation from the Member’s medical records maintained by the requesting independent practitioner’s office verifying the following:

6.1 Member had adequate response to previously administered doses of Ruconest; AND

6.2 All criteria for initial therapy are met;

6.3 If criteria are met, approve for a maximum of six (6) vials in any one (1) month for a maximum of three (3) months.

References:

