Status
Active

Medical and Behavioral Health Policy
Section: Medicine
Policy Number: II-102
Effective Date: 03/26/2014

TREATMENT OF HEREDITARY ANGIOEDEMA

Description:

Hereditary angioedema (HAE) is a rare autosomal dominant disease caused by a deficiency of C1 inhibitor, which helps control inflammation. It is characterized by recurrent episodes of angioedema without urticaria or pruritus that often affect the skin or the mucosal tissues of the upper respiratory and gastrointestinal tracts. HAE is distinct from other more common forms of angioedema, which have a variety of causes including allergies and drug sensitivities. Criteria used to confirm diagnosis of HAE are included in the policy statement. Genetic testing is not needed to confirm a diagnosis of HAE.

Triggers for attacks of HAE may vary, but can include minor trauma or stress. Episodes often occur without a defined precipitating factor. HAE attacks result in progressive swelling without erythema over the first 24 hours and then gradually subside during the following 48 to 72 hours. Although the swelling is self-limited, laryngeal involvement may cause fatal asphyxiation.

Agents currently used for prophylaxis and/or treatment of acute attacks of HAE include:

- **17 alpha-alkylated androgen**
  Danazol (Danocrine®): oral agent FDA-approved for long-term prophylaxis of HAE and unlabeled use for short-term prophylaxis of HAE.
- **Antifibrinolytic**
  Tranexamic acid (Lysteda™): oral agent for unlabeled use as short- and long- term prophylaxis and treatment of acute HAE.
- **C1 esterase inhibitors**
  - Cinryze®: intravenous agent FDA-approved for routine prophylaxis against HAE attacks in adolescent and adult patients. Cinryze is FDA-approved for self-administration.
  - Berinert®: intravenous agent FDA-approved for acute abdominal or facial attacks of HAE in adult and adolescent patients who may self-administer if appropriately trained.

- **Plasma kallikrein inhibitor**
  Ecallantide (Kalbitor®): subcutaneous injection FDA-approved for treatment of acute attacks of HAE in patients 16 years of age and older. Ecallantide is not FDA-approved for self-administration.
- **Bradykinin B2 receptor antagonist**
  Icatibant (Firazyr®): subcutaneous injection FDA-approved for treatment of acute attacks of HAE in adults 18 years of age and older. Icatibant is FDA-approved for self-administration.

Policy:

Prior to use of **any** pharmacologic agent, the patient must have a diagnosis of hereditary angioedema (HAE) confirmed by:

- At least one of the following clinical manifestations:
  1. Recurrent self-limiting, non-inflammatory subcutaneous angioedema without urticaria lasting more than 12 hours; OR
  2. Recurrent, self-remitting abdominal pain without clear organic etiology lasting more than six hours; OR
  3. Recurrent laryngeal edema;

  AND
- Laboratory values on two separate occasions demonstrating one of the following:
  1. Low C1 Inhibitor level and low C1 inhibitor function (HAE Type I); OR
  2. Normal C1 Inhibitor level and low C1 inhibitor function (HAE Type II).

Treatment of acute attacks:

If the criteria for HAE diagnosis are met, pharmacologic treatment may be considered **MEDICALLY NECESSARY** for the treatment of acute attacks in patients with:

- Laryngeal or facial edema; OR
- Severe abdominal attacks;

  AND
- Only drugs which are FDA-approved for these indications are used (i.e., Berinert®, Kalbitor® or Firazyr®).

Short-term prophylaxis:

If the criteria for HAE diagnosis are met, pharmacologic treatment may be considered **MEDICALLY NECESSARY** prior to surgery, invasive medical procedures, or substantial dental procedures, such as tooth extractions, for short-term prophylaxis against angioedema attacks in patients with a history of laryngeal edema. Drugs used include androgens (e.g., danazol, stanozolol) and antifibrinolytics (tranexamic acid).

Long-term prophylaxis:

If the criteria for HAE diagnosis are met, pharmacologic treatment may be considered **MEDICALLY NECESSARY** for long-term prophylaxis against angioedema attacks for adult and adolescent patients:

- Who experience greater than one severe attack per month or are disabled more than 5 days per month or have laryngeal attacks.
  AND
- Have a documented trial and failure, contraindication, or intolerance to a 17-alpha alkylated androgen (e.g., danazol) or anti-fibrinolytic agents (e.g. tranexamic acid).
  AND
- Only drugs which are FDA-approved for these indications are used (i.e., Danocrine® or Cinryze®).

Use of a C1 esterase inhibitor (i.e., Cinryze®, Berinert®), plasma kallikrein inhibitor (i.e., Kalbitor®), or bradykinin B2 receptor antagonist (i.e., Firazyr®) is considered **INVESTIGATIVE** for all other indications, including but not limited to, use as a diagnostic agent to distinguish abdominal attacks of C1 inhibitor disorders from other abdominal pathologies.

The combined use of a C1 Esterase Inhibitor (i.e., Cinryze®, Berinert®) and a plasma kallikrein inhibitor (i.e., Kalbitor®) is considered **INVESTIGATIVE**.

Coverage:

Blue Cross and Blue Shield of Minnesota medical policies apply generally to all Blue Cross and Blue Plus plans and products. Benefit plans vary in coverage and some plans may not provide coverage for certain services addressed in the medical policies.

Medicaid products and some self-insured plans may have additional policies and prior authorization requirements. Receipt of benefits is subject to all terms and conditions of the member's summary plan description (SPD). As applicable, review the provisions relating to a specific coverage determination, including exclusions and limitations. Blue Cross reserves the right to revise, update and/or add to its medical policies at any time without notice.

For Medicare NCD and/or Medicare LCD, please consult CMS or National Government Services websites.

Refer to the Pre-Certification/Pre-Authorization section of the Medical Behavioral Health Policy Manual for the full list of services, procedures, prescription drugs, and medical devices that require Pre-certification/Pre-Authorization. Note that services with specific coverage criteria may be reviewed retrospectively to determine if criteria are being met. Retrospective denial of claims may result if criteria are not met.

Coding:

The following codes are included below for informational purposes only, and are subject to change without notice. Inclusion or exclusion of a code does not constitute or imply member coverage or provider reimbursement.

HCPCS:

J0597 Injection, C-1 esterase inhibitor (human), berinert, 10 units
J0598 Injection, C-1 esterase inhibitor (human), cinryze, 10 units
J1290 Injection, ecallantide, 1 mg
J1744 Injection, icatibant, 1 mg
J3490 Unclassified drugs
J3590 Unclassified biologics
J8499 Prescription drug, oral, nonchemotherapeutic, NOS

Policy History:

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Reviewed March 9, 2011
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Cross Reference: