Policy Subject: Hereditary Angioedema Agents

Policy Number: SHS PBD21

Category:

Policy Type: [ ] Medical [ ] Pharmacy

Department: Pharmacy

Dates:

Effective Date: October 28, 2010
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Approval Date: October 25, 2017
Next Review Date: October 2018

Product (check all that apply):
[ ] Group HMO/POS
[ ] Individual HMO/POS
[ ] PPO
[ ] ASO

Clinical Approval By:

Medical Directors
PHP: Peter Graham, MD; SPHN: Harman Nagler, MD

Pharmacy and Therapeutics Committee
PHP: Peter Graham, MD; Sparrow ASO: Harman Nagler, MD

Policy Statement:

Physicians Health Plan, PHP Insurance & Service Company, and Sparrow PHP will cover Hereditary angioedema agents through the Medical Benefit based on approval by the Clinical Pharmacist or Medical Director using the following determination guidelines

Drugs and Applicable Coding:

J-code: Cinryze - J0598; Berinert - J0597, J1290; Kalbitor - J2425; Firazyr - 014778; Ruconest - J0596

Clinical Determination Guidelines:

Document the following with chart notes

A. Hereditary Angioedema (HAE)
1. Diagnosis and Severity
   a. Age:
      • Berinert (C1 Estrase Inhibitor Human IV), Cinryz (C1 Inhibitor Human, IV), Ruconest (C1 estrase Inhibitor, recombinant IV), Haegarda (C1 Inhibitor Human SC):
         Adolescents & adults
      • Firazyr (icatibant): ≥ 18 yo
      • Kalbitor (ecallantide): ≥ 16 yo
   b. Prescriber/consultant: Allergist, immunologist or hematologist
   c. Severity: Swelling of face/throat or GI tract that notably interferes w routine daily activities.
   d. Lab test: both below
      • C4: <14mg/L (normal 9-36 mg/dL)
      • C1 Inhibitor (antigenic) <19.9mg/dL (normal 21-39mg/dL) or C1 Inhibitor (functional) <72% reference range (normal >67% reference range)
   e. Concomitant medications: Meds known to cause angioedema (ie. ACE inhibitors, estrogens, ARBs) have been evaluated & D/c’ed when appropriate
Pharmacy Benefit Determination Policy

B. Acute HAE treatment
   1. Administration:
      a. Self-administration: Berinert, Firazyr, & Ruconest after training by healthcare professional
      b. Healthcare professional administration: Kalbitor
   2. Dosage Regimen:
      a. Berinert (plasma-derived C1 INH IV): 20U/Kg
      b. Ruconest (recombinant C1 INH IV): < 84 Kg: 50 U/KG, > 84 Kg: 4,200 U; May repeat X1
      c. Kalbitor (ecallantide SC): 30mg (3 x 1mL)
      d. Firazyr (icatibant SC): 30mg
   3. Approval:
      a. Initial: 6 months;
      b. Re-approval: 1 yr.; quantity dependent on frequency of attacks (↓ severity & duration of attacks)

C. Prophylactic HAE treatment
   1. Diagnosis & Severity:
      a. Frequent & severe HAE attacks: > 24 days/yr w sx or > 12 severe attacks/yr.
      b. Severe HAE attacks in triggering situations: Major dental work, surgical procedures or invasive medical procedures
   2. Other therapies: Failure or contraindication/significant adverse effects from 1 below:
      a. Acute HAE treatment (B)
      b. Attenuated androgens: danazol, stanozolol
   3. Dosage regimen
      a. Cinryz (C1 Inhibitor Human IV): 1,000 q 3-4 days
      b. Haegarda (C1 Inhibitor Human SC): 60U/Kg q 3-4 days
   4. Approval
      a. Initial: 6 months
      b. Re-approval: 1 yr. (functional improvement w ↓ frequency, severity & duration of attacks)
## Appendix I: Monitoring & Patient Safety

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<th>Drug</th>
<th>Adverse Reactions</th>
<th>Monitoring</th>
<th>REMS</th>
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| Berinert Cinryze Haegarda plasma C1-INH | • CNS: HA (17%)  
• GI: Nausea (18%)  
• Preg.: Animal reproductive studies have not been conducted | • CV: S & Sx thrombolytic events  
• Immunologic: S & Sx hypersensitivity | Not needed |
| Kalbitor ecallantide        | • CNS: HA (8-16%), fatigue (12%)  
• GI: Nausea (5-13%), diarrhea (4-11%)  
• Immunologic: Antibody development (IgE: 5-20%, neutralizing: 9%)  
• Preg.: Adverse effects were observed in animal studies | • Immunologic: S & Sx hypersensitivity | REMS program  
Dc’ed by  
FDA April 2013 |
| Firazyr icatibant           | • Derm.: Inj. site Rx (97%),  
• Preg.: Adverse effects were observed in animal studies | • Symptoms relief laryngeal sx/airway obstruction | Not needed |
| Ruconest recombinant C1 INH | • CNS: HA (>10%)  
• GI: Abdominal pain (>12%)  
• Resp.: Oropharyngeal (>12%) | • CV: S & Sx thrombolytic events  
• Misc: S & Sx hypersensitivity | Not Needed |

### References and Resources:

1. Lexicomp Online®, Lexi-Drugs®, Hudson, Ohio: Lexi-Comp, Inc.; Berinert, Cinryze, Haegarda; Firayz; Ruconest, Kalbitor accessed August 2017
10. Review of recent guidelines and consensus statements on hereditary angioedema therapy with focus on self-administration Int Arch Allergy Immunol. 2013;16(suppl 1):3-9
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<th>Approved By:</th>
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<tr>
<td>Peter Graham, MD – PHP Executive Medical Director</td>
<td>10/25/17</td>
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<tr>
<td>Harman Nagler, MD – SPHN Executive Medical Director</td>
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<td>Human Resources</td>
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