

Pharmacy Benefit Determination Policy

Policy Subject: Hereditary Angioedema Agents Policy Number: SHS PBD21 Category: Policy Type: <input checked="" type="checkbox"/> Medical <input type="checkbox"/> Pharmacy Department: Pharmacy	Dates: Effective Date: October 28, 2010 Revision Date: November 13, 2018 Approval Date: October 25, 2017 Next Review Date: October 2018
Product (check all that apply): <input checked="" type="checkbox"/> Group HMO/POS <input checked="" type="checkbox"/> Individual HMO/POS <input checked="" type="checkbox"/> PPO <input checked="" type="checkbox"/> ASO	Clinical Approval By: Medical Directors PHP: Peter Graham, MD Pharmacy and Therapeutics Committee PHP: Peter Graham, 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
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Drugs and Applicable Coding: J-code: Cinryze - J0598; Berinert - J0597, J1290; Kalbitor - J2425; Firazyr - 014778; Ruconest - J0596 Takhzyro - pending
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Clinical Determination Guidelines: Document the following with chart notes A. Hereditary Angioedema (HAE) 1. Age: a. Berinert IV (C1 Estrase Inhibitor Human), Cinryz IV (C1 Inhibitor Human), Ruconest IV (C1 estrase Inhibitor, recombinant), Haegarda SC (C1 Inhibitor Human): Adolescents and adults b. Firazyr (icatibant): ≥ 18 years c. Kalbitor (ecallantide): ≥ 16 years d. Haegarda (C1 Inhibitor Human): e. Takhzyro (lanadelumab-flyo): ≥ 12 years 2. Prescriber: Allergist, immunologist or hematologist 3. Diagnosis and severity a. Lab test: both below <ul style="list-style-type: none"> • C4: $<14\text{mg/L}$ (normal 9-36 mg/dL) • C1 Inhibitor (antigenic) $<19.9\text{mg/dL}$ (normal 21-39mg/dL) <u>or</u> C1 Inhibitor (functional) $<72\%$ reference range (normal $>67\%$ reference range) b. Severity: Swelling of face/throat or GI tract that notably interferes with routine daily activities. c. Concomitant medications: Medications known to cause angioedema (ie. ACE inhibitors, estrogens, ARBs) have been evaluated and discontinued when appropriate

Pharmacy Benefit Determination Policy

- B. Acute HAE treatment
 - 1. Administration:
 - a. Self-administration: Berinert, Firazyr and Ruconest after training by healthcare professional
 - b. Healthcare professional administration: Kalbitor
 - 2. Dosage regimen:
 - a. Berinert IV (plasma-derived C1 INH): 20U/Kg
 - b. Ruconest IV (recombinant C1 INH): < 84 Kg: 50 U/KG, ≥ 84 Kg: 4,200 U; may repeat x 1
 - c. Kalbitor SC (ecallantide): 30mg (3 x 1mL)
 - d. Firazyr SC (icatibant): 30mg
 - 3. Approval:
 - a. Initial: 6 months;
 - b. Re-approval: 1 year; quantity dependent on frequency of attacks (decreased severity and duration of attacks)
- C. Prophylactic HAE treatment
 - 1. Diagnosis and severity:
 - a. Frequent and severe HAE attacks: > 24 days/year with symptoms or > 12 severe attacks/year.
 - b. Severe HAE attacks in triggering situations: Major dental work, surgical procedures or invasive medical procedures
 - 2. Other therapies: Failed or contraindication/significant adverse effects from 1 below:
 - a. Acute HAE treatment (see B)
 - b. Attenuated androgens: danazol, stanozolol
 - 3. Dosage regimen
 - a. Cinryz IV (C1 Inhibitor Human): 1,000U every 3-4 days
 - b. Haegarda SC (C1 Inhibitor Human): 60U/Kg every 3-4 days
 - c. Takhzyro SC (lanadelumab-flyo): 300mg every 2 weeks
 - 4. Approval
 - a. Initial: 6 months
 - b. Re-approval: 1 year (functional improvement with decreased frequency, severity and duration of attacks)

Pharmacy Benefit Determination Policy


Appendix I: Monitoring & Patient Safety

Drug	Adverse Reactions	Monitoring	REMS
Berinert IV Cinryze IV Haegarda SC plasma C1-INH	<ul style="list-style-type: none"> • CNS: HA (17%) • GI: Nausea (18%) • Preg.: Animal reproductive studies have not been conducted 	<ul style="list-style-type: none"> • CV: S & Sx thrombolytic events • Immunologic: S & Sx hypersensitivity. 	Not needed
Kalbitor ecallantide	<ul style="list-style-type: none"> • 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 	<ul style="list-style-type: none"> • Immunologic: S & Sx hypersensitivity 	REMS program Dc'ed by FDA April 2013
Takhzyro SC lanadelumab-flyo	<ul style="list-style-type: none"> • CNS: HA (33%) • Immunologic: antibody development (12%) • Local: Injection site reaction (45-56%) • MSK: Myalgia (11%) • Resp: URI (44%) 	<ul style="list-style-type: none"> • NA 	Not needed
Firazyr SC icatibant	<ul style="list-style-type: none"> • Derm.: Inj. site Rx (97%), • Preg.: Adverse effects were observed in animal studies 	<ul style="list-style-type: none"> • Symptoms relief laryngeal sx/airway obstruction 	Not needed
Ruconest IV recombinant C1 INH	<ul style="list-style-type: none"> • CNS: HA (>10%) • GI: Abdominal pain (≥12%) • Resp.: Oropharyngeal (≥12%) 	<ul style="list-style-type: none"> • CV: S & Sx thrombolytic events • Misc: S & Sx hypersensitivity 	Not Needed

References and Resources:

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	10/25/17
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