Pharmacy Benefit Determination Policy

Policy Subject: PAH Drugs	**Dates:**
Policy Number: SHS PBD26	**Effective Date:** June 24, 2010
Category: Respiratory	**Revision Date** November 13, 2018
Policy Type: ☒ **Medical** ☒ **Pharmacy**	**Approval Date:** December 5, 2018
Department: Pharmacy	**Next Review Date:** December 2019
Product (check all that apply):	**Clinical Approval By:**
☒ Group HMO/POS	**Medical Directors**
☒ Individual HMO/POS	PHP: Peter Graham, MD
☒ PPO	**Pharmacy and Therapeutics Committee**
☒ ASO	PHP: Peter Graham, MD

Policy Statement:

Physicians Health Plan, PHP Insurance & Service Company, and Sparrow PHP will cover PAH medications (Endothelial Receptor Antagonist (ERA), Guanylate Cyclase (sGC) Stimulant, Phosphodiesterase Inhibitors (PDE-5i), or Prostanoids) through the Medical/Pharmacy Benefit based on approval by the Clinical Pharmacist or Medical Director using the following determination guidelines

Drugs and Applicable Coding:

J-Code: Flolan/Veletri - J1325; Remodulin - J3285; Tyvaso - J7686; Ventavis - Q4074

Clinical Determination Guidelines:

Document the following with chart notes

A. Pulmonary Arterial Hypertension (PAH)
   1. Diagnosis and severity:
      a. Prescriber: Cardiologist or pulmonologist
      b. WHO or NYHA rating scale (see Appendix I)
      c. Heart catherization or echocardiogram: Mean pulmonary artery pressure (mPAP) > 25 mmHg
   2. Vasoreactivity test
      a. Completed or documented inappropriateness to vasoreactivity test
      b. Positive test: Decrease mPAP $\geq$ 10mmHg, to mPAP $\leq$ 30mmHg, with unchanged or increased cardiac output

B. Vaso-reactive PAH
   1. Diagnosis and Severity: NYHA I-III (see Appendix I)
   2. Other therapies: Failed or had significant adverse effects from 1 calcium channel blocker - Nifedipine XL: 40 -120mg/day; Diltiazem: 30 - 90mg 3x/day; Amlodipine: 4 - 40mg/day
   3. Preferred drug step therapy (see Appendix II)
      a. Revatio (sildenafil po): Failed or significant adverse effects to calcium channel blocker
      b. Other oral PAH agents: Failed or significant adverse effects from sildenafil
      c. Non-oral PAH agents: Failed or significant adverse effects to 2 oral agents

C. Non-vasoreactive PAH (see Appendix I & II)
   1. NYHA IV or
   2. NYHA II or III (1 of the below)
      a. Revatio (sildenafil po): Approve generic sildenafil
      b. Other oral PAH agents: Failed or significant adverse effects from sildenafil
      c. Non-oral PAH agents: Failed or significant adverse effects to 2 oral agents

D. Combination Therapy
   1. Severity: Considered for patients who fail to show improvement or who deteriorate w mono-therapy
   2. Other therapies: Trial of agents before adding another agent or changing classes
      a. Initial oral regimen: 3-6 months
      b. Combination therapy: 1 month
   3. Combinations (see Appendix II)
      a. Two agents:
         - ERA + PDE-5i;
         - Prostanoid + ERA;
         - Prostanoid + PDE-5i;
         - ERA + sGC stimulant;
         - sGC stimulant + prostanoid
      b. Three agents:
         - ERA + prostanoid + PDE-5i;
         - ERA + Prostanoid + sGC stimulant
   4. Monitoring parameter for those not achieving goals with monotherapy:
      a. Symptoms worsening with signs of heart failure
      b. Echocardiogram shows right ventricular enlargement
      c. Tests:
         - Increased right arterial pressure (RAP) and decreased cardiac index (CI);
         - Increased B-type natriuretic peptide (BNP)
         - Decreased six-minute walk distance (6MWD)

E. Approval
   1. Initial: 6 months
   2. Re-approval: 1 year (Decreased or stabilize NYHA/WHO functional class and/or decreased or stabilize MPAP)

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Appendix I: Classifications of Pulmonary Hypertension (WHO and NYHA)

Class	Limits	WHO	NYHA
I	No limitation	Ordinary physical activity doesn't cause undue dyspnea/fatigue, chest pain, or near syncope	Ordinary physical activity doesn't cause symptoms
II	Slight limitation	Comfortable at rest Ordinary physical activity causes undue dyspnea/fatigue, chest pain, or near syncope.	Comfortable at rest Ordinary physical activity causes symptoms
III	Marked limitation	Comfortable at rest Less than ordinary activity causes undue dyspnea/fatigue, chest pain, or near syncope.	Comfortable at rest Less than ordinary activity causes symptoms
IV	Inability to carry on any physical activity	Dyspnea and/or fatigue may even be present at rest. Discomfort is ↑ed by any physical activity.	Symptoms present at rest

Appendix II: Agents used for Pulmonary Hypertension

Class	Agent	Class	Dosage
Endothelial Receptor Antagonist (ERA)	Letaris (ambrisentan po)	WHO II, III	Initial: 5mg 1x/day Maximum: 10mg 1x/day
	Opsumit (macitentan po)	WHO II, III	10mg 1x/day
	Tracleer (bosentan)	NYHA II, III, IV	Initial: 62.5mg 2x/day x 4 wks. Maintenance: 125mg 2x/day (>40Kg)
Guanylate Cyclase (sGC) Stimulant	Adempas (riociguat po)	WHO II, III	1mg po 3x/day
Phosphodiesterase Inhibitors (PDE-5i)	Adcirca (tadalafil po)	NYHA II, III	40mg 1x/day
	Revatio (sildenafil po)	NYHA II, III	5mg or 20mg 3x/day
Prostanoids	Uptravi (selexipag po)	WHO II, III	Initial: 200mcg 2x/day Titration:
	Orenitram (treprostinil po)	WHO II, III	Initial: 0.25mg q 12hrs Titration: ↑ 0.25-0.5mg q 3-4 days
	Tyvaso (treprostinil Inhalation)	NYHA III	Initial: 18mcg (3 inhalations) q 4hrs 4x/day Titration: ↑ 3 inhalations q 1-2wk Maintenance:54mcg (9 inhalations) 4x/day
	Remodulin (treprostinil SC)	NYHA II, III, IV	Initial: 1.25ng/Kg/min. Titration: ↑ 1.25ng/kg/min/wk x 4 wks ↑ 2.5ng/Kg/min/wk thereafter
	Flolan /Veletri (epoprostenol IV)	NYHA III, IV	Initial: 2ng/Kg/min. infusion Titration: ↑ 1-2ng/Kg/min. q ≥15 mins. Maximum: 195ng/Kg/min.
	Ventavis (iloprost inhalation)	NYHA III, IV	Initial: 2.5mcg/inhalation Maintenance: 2.5-5mcg/inhalation 6-9x/day

Appendix III: Monitoring & Patient Safety

Drug	Adverse Reactions	Monitoring	REMS
Endothelial Receptor Antagonist (ERA) Letaris Tracleer Opsumit	• CV: Peripheral edema (11-29%) • CNS: HA (14-15%) Heme: Anemia (11-13%), • Resp: Resp. tract infection (20-22%), • Pregnancy category X	• CV: S & Sx of peripheral edema • Hepatic: LFT's pre & during; liver injury S & Sx • Hem: Hgb/Hct prior & during therapy • Pregnancy Test: pre/post & monthly during	• Purpose: Warn re preg. precautions • Prescribers & Rx: Enrolled in Opsumit, Tracleer, Latairis REMS, read medication guide & review preg. tests • Med. guide: Dispense w product • Web sites: http://www.opsumitrems.com/, http://www.tracleer.com/Hcp-Healthcare-Professionals , http://www.letairisrems.com/REMS_Program.aspx (https://www.adempasrems.com).
Guanylate Cyclase (sGC) Stimulant Adempas	• CV: Hypotension (3-10%) • CNS: HA (27%), dizziness (20%), • GI: Dyspepsia (13-19%), N/V (10-14%), diarrhea (12%), • Pregnancy category X	• CV: BP, peripheral edema S & Sx • Resp. ↑function, PFT exercise tolerance • Pregnancy Test: Pre/post & monthly during	
Phosphodiesterase Inhibitors (PDE-5i) Revatio Adcirca	• CV: Flushing (1-19%) • CNS: HA (3-46%) • GI: Dyspepsia (1-17%), nausea (10-11%) • Neuro/MSK: Myalgia (1-14%), back/extremity pain (1-12%) • Resp: Resp tract inf. (3-13%), epitaxis (9-13%) • Pregnancy category B	• Response to therapy • CV: Blood pressure, HR • Resp: Pulmonary edema S & Sx	• Not needed
Prostanoids Flolan/Veletri Ventavis Remodulin Tyvaso Uptravi Orenitram	• CV: ↑ HR (35-43%), flushing (23-42%), hypotension (13%) • CNS: Dizziness (83%), HA (46-83%), chills (25%), fever (25%), flu-like Sx (25%), Sepsis (25%), anxiety (21%), tremor (21%), agitation (11%) • Derm: Ulcer (39%), eczema (25%), skin rash (25%), urticarial (25%) GI: Diarrhea (25%), nausea (22-41%) • Local: Infusion pain (85%), site rx (83%) • Misc.: Jaw pain (13-54%) • Pregnancy category B	• CV: BP, HR • Local: Infusion site symptoms	• Not needed

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Approved By:

12/5/18

Peter Graham, MD – PHP Executive Medical Director — Date

12/5/18

Human Resources – Kurt Batteen — Date