MEDICAL POLICY STATEMENT		
Effective Date	**Next Annual Review Date**	**Last Review / Revision Date**
06/15/2011	**5/13/2015**	**5/13/2014**
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CareSource

CSMG Medical Policy Statements are derived from literature based and supported clinical guidelines, nationally recognized utilization and technology assessment guidelines, other medical management industry standards, and published MCO clinical policy guidelines. Medically necessary services are those health care services or supplies which are proper and necessary for the diagnosis or treatment of disease, illness, or injury and without which the patient can be expected to suffer prolonged, increased or new morbidity, impairment of function, dysfunction of a body organ or part or significant pain and discomfort. These services meet the standards of good medical practice in the local area, are the lowest cost alternative and are not provided mainly for the convenience of the member or provider.

A. SUBJECT

Pulmonary Arterial Hypertension

Endothelin Receptor Antagonist

- **Ambrisentan (Letairis)**
- **Bosentan (Tracleer)**

Phosphodiesterase Type 5 inhibitors

- **Tadalafil (Adcirca)**
- **Sildenafil citrate (Revatio) Oral and Infusion**
- **riociguat (Adempas)**

Peripheral Vasodilators

- **Treprostinil (Remodulin) Infusion**
- **Treprostinil (Tyvaso) Inhalation**
- **Epoprostenol (Flolan, Veletri) Infusion**
- **Iloprost (Ventavis) Inhalation**

B. BACKGROUND

The CareSource Medication Policies are therapy class policies that are used as a guide when determining health care coverage for our members with benefit plans covering prescription drugs. Medication Policies are written on selected prescription drugs requiring prior authorization or Step-Therapy. The Medication Policy is used as a tool to be interpreted in conjunction with the member's specific benefit plan.

The intent of the pulmonary arterial hypertension (PAH) Program is to encourage appropriate selection of patients for therapy according to product labeling and/or clinical guidelines and/or clinical studies, and also to encourage use of preferred agents.

C. POLICY

CareSource will approve the use of ambrisentan (Letairis) and bosentan (Tracleer), Tadalafil (Adcirca), Sildenafil citrate (Revatio) Oral and Infusion, Adempas (riociguat), Treprostinil

(Remodulin) Infusion, Treprostinil (Tyvaso) Inhalation, Epopostenol (Flolan, Veletri) Infusion, Iloprost (Ventavis) Inhalation and consider their use as medically necessary when the following criteria have been met for:

- Pulmonary arterial hypertension

Endothelin Receptor Antagonist

- **Ambrisentan** (Letairis) and **bosentan** (Tracleer) are indicated for the treatment of pulmonary arterial hypertension (WHO Group 1) to improve exercise ability and delay clinical worsening.

- **Ambrisentan** (Letairis) studies establishing effectiveness included predominantly patients with WHO Functional Class II-III symptoms and etiologies of idiopathic or heritable PAH (64%) or PAH associated with connective tissue diseases (32%).

- **Bosentan** (Tracleer) studies establishing effectiveness included predominately patients with NYHA Functional Class II-IV symptoms and etiologies of idiopathic or heritable PAH (60%), PAH associated with connective tissue diseases (21%), and PAH associated with congenital systemic-to-pulmonary shunts (18%).

Prior Authorization Criteria:

- Documented diagnosis of pulmonary arterial hypertension
  - WHO Group 1 with NYHA class II or III for Letairis or II through IV symptoms for Tracleer
  - Pulmonary arterial pressure not adequately controlled using an oral vasodilator (e.g. calcium channel blockers) at
    - maximal doses OR the member was not vasodilator sensitive as determined by an epoprostenol, adenosine, or inhaled nitric oxide challenge.
- Patient must be 18 years or older
- Prescribed by a pulmonologist and/or cardiologist or under recommendation of pulmonologist and/or cardiologist

Phosphodiesterase Type 5 inhibitors

- **Tadalafil** (Adcirca) and **sildenafil citrate** (Revatio) are indicated for the treatment of pulmonary arterial hypertension (PAH) (WHO Group 1) to improve exercise ability and delay clinical worsening. Studies establishing effectiveness included predominately patients with NYHA Functional Class II – III symptoms and etiologies of idiopathic or heritable PAH (61%-Adcirca) (71%-Revatio) or PAH associated with connective tissue diseases (23%-Adcirca)/ (25%-Revatio).

Prior Authorization Criteria:

- Documented diagnosis of pulmonary arterial hypertension
  - WHO Group 1 with NYHA Functional class II or III symptoms.
  - PAP pressures not adequately controlled using an oral vasodilator (e.g. calcium channel blocker) at maximal doses
    - **OR**
  - The member was not vasodilator sensitive as determined by an epoprostenol, adenosine, or inhaled nitric oxide challenge.
- Patient must be 18 years or older
- Prescribed by a pulmonologist and/or cardiologist or under recommendation of Functional Assessment of Pulmonary Arterial Hypertension

Peripheral Vasodilators

- **Epoprostenol sodium,** Prostacyclin, PGI2, Veletri®, Flolan® continuous intravenous infusion is considered **medically necessary** as a treatment for individuals who meet **all** of the following criteria:
  - Age 18 years or older

    AND
  - Pulmonary hypertension, as indicated by **1 or more** of the following
    - Idiopathic or heritable pulmonary arterial hypertension
    - Pulmonary arterial hypertension associated with scleroderma spectrum of diseases

    AND
  - Treatment as indicated by:
    - New York Heart Association or World Health Organization functional class III symptoms and patient has not responded to specific oral therapies for pulmonary hypertension (e.g., bosentan, sildenafil)

      OR
    - New York Heart Association or World Health Organization functional class IV symptoms

- **Treprostinil sodium,** Remodulin® continuous subcutaneous infusion and continuous intravenous infusion is considered **medically necessary** as a treatment for individuals who meet **all** of the following criteria:

  - Age 18 years or older
  - Transition from another therapy for pulmonary arterial hypertension needed, as indicated by **1 or more** of the following
    - Who are either not candidates for or have failed to respond to oral calcium channel blocker therapy
    - Who are not candidate for or has failed to respond to other oral medications (e.g., ambrisentan, bosentan, sildenafil, tadalafil)
    - Patient requires transition from epoprostenol.
  - World Health Organization group 1 pulmonary arterial hypertension, associated with 1 or more of the following:
    - Chronic hemolytic anemia
    - Congenital heart disease
    - Connective tissue diseases, including systemic sclerosis
    - Drugs or toxins (e.g., fenfluramine, methamphetamine, cocaine)
    - Family history, including mutation in BMPR2 gene
    - HIV infection
    - Idiopathic pulmonary arterial hypertension
    - Portal hypertension
    - Pulmonary capillary hemangiomatosis
    - Pulmonary veno-occlusive disease
    - Schistosomiasis

- **Iloprost** (Ventavis®) Inhalation Solution or TYVASO™ Inhalation Solution***** (treprostinil) is considered **medically necessary** as a treatment for individuals who meet **all** of the following criteria:

- Age 18 years or older
- New York Heart Association or World Health Organization functional class III or IV symptoms [B]
- Patient has received but not adequately responded to conventional treatment (e.g., oxygen, anticoagulants, calcium channel blockers, diuretics).
- World Health Organization group 1 pulmonary arterial hypertension, [C] associated with 1 or more of the following:
    - Chronic hemolytic anemia
    - Congenital heart disease
    - Connective tissue diseases, including systemic sclerosis
    - Drugs or toxins (e.g., fenfluramine, methamphetamine, cocaine)
    - Family history, including mutation in BMPR2 gene
    - HIV infection
    - Idiopathic pulmonary arterial hypertension
    - Portal hypertension
    - Pulmonary capillary hemangiomatosis
    - Pulmonary veno-occlusive disease
    - Schistosomiasis

Functional Assessment of Pulmonary Arterial Hypertension

New York Heart Association functional classification	
Class 1:	Cardiac disease, but no symptoms and no limitation in ordinary physical activity, e.g. shortness of breath when walking, climbing stairs etc.
Class 2:	Mild symptoms (mild shortness of breath and/or angina) and slight limitation during ordinary activity.
Class 3:	Marked limitation in activity due to symptoms, even during less-than-ordinary activity, e.g. walking short distances (20–100 m). Comfortable only at rest.
Class 4:	Severe limitations. Experiences symptoms even while *at rest*. Mostly bedbound patients
World Health Organization functional assessment classification	
Class I:	Patients with PH but without resulting limitation of physical activity. Ordinary physical activity does not cause undue dyspnea or fatigue, chest pain, or near syncope.
Class II:	Patients with PH resulting in slight limitation of physical activity. They are comfortable at rest. Ordinary physical activity causes undue dyspnea or fatigue, chest pain, or near syncope.
Class III:	Patients with PH resulting in marked limitation of physical activity. They are comfortable at rest. Less than ordinary activity causes undue dyspnea or fatigue, chest pain, or near syncope.
Class IV:	Patients with PH with inability to carry out any physical activity without symptoms. These patients manifest signs of right-heart failure. Dyspnea and/or fatigue may even be present at rest. Discomfort is increased by any physical activity.

All other uses of PAH agents above **are considered experimental/investigational and therefore, will follow CareSource's off label policy.**

Note: Documented diagnosis must be confirmed by portions of the individual's medical record which will confirm the presence of disease and will need to be supplied with prior authorization request. These medical records may include, but not limited to test reports, chart notes from provider's office or hospital admission notes.

Refer to the product package insert for dosing, administration and safety guidelines.

Conditions of Coverage

J-Code	**J3285** - treprostinil (Remodulin) **J3490** - iloprost (Ventavis) **J1325** - epoprostenol (Flolan, Veletri) **J7686** - treprostinil, inhalation solution (Tyvaso)
Place Of Service	Office, Outpatient, Home *****Preferred place of service is in the home*.** This medication can be self-administered and can be billed through the pharmacy benefit. **Note:** CareSource supports administering inject able medications in various setting, as long as those services are furnished in the most appropriate and cost effective setting that are supportive of the patient's medical condition and unique needs and condition. The decision on the most appropriate setting for administration is based on the member's current medical condition and any required monitoring or additional services that may coincide with the delivery of the specific medication.
Authorization Period	Approved authorizations are valid for 1 year. Continued treatment may be considered when the member has shown biological response to treatment. ALL authorizations are subject to continued eligibility

D. REVIEW / REVISION HISTORY

5/2014 – combined all PAH agents to one policy

E. REFERENCES

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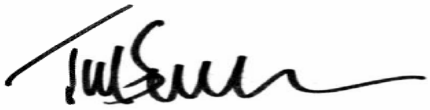
The medical Policy Statement detailed above has received due consideration as defined in the Medical Policy Statement Policy and is approved.

5/13/2014

Chief Medical Officer **Date**



5/1/2014

Director of Specialty Pharmacy **Date**

Independent Medical Review 2011