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1.0 Description of the Procedure, Product, or Service

Pulmonary Hypertension (PH)

PH refers to the presence of abnormally high pulmonary vascular pressure. The World Health Organization (WHO) classifies patients with PH into five groups based on etiology. These groups differ in their clinical presentation, diagnostic findings, and response to treatment. It is important to note the changes in defining and classifying pulmonary hypertension in the following revised WHO Classification of PH developed by the 2009 American College of Cardiology Foundation/American Heart Association (ACCF/AHA) 2009 Expert Consensus Task Force on Pulmonary Hypertension.

Patients in Group 1 are considered to have Pulmonary Arterial Hypertension (PAH), and the remaining four groups are considered to have PH.

Revised WHO Classification of Pulmonary Hypertension(PH)

- a. Pulmonary arterial hypertension (PAH)
 1. Idiopathic (IPAH)
 2. Familial (FPAH)
 3. Associated with (APAH)
 - (a) Connective tissue disorder
 - (b) Congenital systemic-to-pulmonary shunts
 - (c) Portal hypertension
 - (d) HIV infection
 - (e) Drugs and toxins
 - (f) Other (thyroid disorders, glycogen storage disease, Gaucher's disease, hereditary hemorrhagic telangiectasia, hemoglobinopathies, chronic myeloproliferative disorders, splenectomy)
 4. Associated with significant venous or capillary involvement
 - (a) Pulmonary veno-occlusive disease (PVOD)
 - (b) Pulmonary capillary hemangiomatosis (PCH)
 5. Persistent pulmonary hypertension of the newborn
- b. Pulmonary hypertension with left heart disease
 1. Left-sided atrial or ventricular heart disease
 2. Left-sided valvular heart disease

- c. Pulmonary hypertension associated with lung diseases and/or hypoxemia
 - 1. Chronic obstructive pulmonary disease
 - 2. Interstitial lung disease
 - 3. Sleep disordered breathing
 - 4. Alveolar hypoventilation disorders
 - 5. Chronic exposure to high altitude
 - 6. Developmental abnormalities
- d. Pulmonary hypertension due to chronic thrombotic and/or embolic disease (CTEPH)
 - 1. Thromboembolic obstruction of proximal pulmonary arteries
 - 2. Thromboembolic obstruction of distal pulmonary arteries
 - 3. Nonthrombotic pulmonary embolism (tumor, parasites, foreign material)
- e. Miscellaneous: Sarcoidosis, histiocytosis X, lymphangiomatosis, compression of pulmonary vessels (adenopathy, tumor, fibrosing mediastinitis)

Pulmonary Arterial Hypertension (WHO Group 1)

Pulmonary Arterial Hypertension (PAH) is a rare and debilitating disease characterized by abnormal proliferation and contraction of pulmonary artery smooth muscle cells. This condition causes a decrease in the size of the pulmonary artery lumen, a decreased reactivity of the vascular bed, increased pulmonary vascular resistance (PVR) and elevated pressure in the pulmonary circulation (initially with normal left-sided pressures) and leads to overload-induced progressive right ventricular dilation and low cardiac output.

Idiopathic pulmonary hypertension (IPAH) is more prevalent in women, and the most common type of PAH. Familial PAH often results from a mutation in bone morphogenetic protein receptor-2 (BMPR2) and is inherited as an autosomal dominant disease. PAH is also associated with congenital heart disease, connective tissue diseases, drugs and toxins, human immunodeficiency virus (HIV), portal hypertension, hemoglobinopathies and myeloproliferative disorders. The diagnosis of PAH requires confirmation with a complete right heart catheterization. The current hemodynamic definition of PAH is a mean pulmonary pressure greater than 25 mmHg; a pulmonary capillary wedge pressure, or left ventricular end-diastolic pressure less than or equal to 15 mmHg; and a pulmonary vascular resistance greater than 3 Wood units.

Non-Pulmonary Arterial Hypertension PH (WHO Groups 2-5)

PH associated with elevated left heart filling pressures are more prevalent than PAH. Treatment should be directed at the underlying left heart disease. Use of PAH-specific treatments for non-PAH PH has been suggested but there are no clinical trial data to support these hypotheses. There are potential adverse side effects of PAH-specific therapies in such patients including increased fluid retention, pulmonary edema, and ventilation perfusion mismatch.

A baseline assessment to determine severity of PAH is often performed before initiation of therapy. This assessment includes the following measures as key determinants of disease severity:

- a. Functional impairment the functional significance of PAH is determined by measuring exercising capacity and determining New York Heart Association (NYHA) or WHO functional class. The WHO functional classification recognizes the importance of near syncope and syncope. Syncope is thought to worsen the prognosis in recipients with PAH. Although not explicitly stated, PAH recipients who have experienced a syncopal episode are generally assigned to WHO Functional Class IV. (See **Subsection 3.3.3**)
- b. Hemodynamic derangement—pulmonary artery systolic pressure and right ventricular function can be estimated by echocardiography. Right heart catheterization is performed to accurately measure the hemodynamic parameters and confirm PAH. Right heart catheterization is often deferred until advanced therapy is indicated because it is an invasive procedure. Recipients with PAH typically undergo an invasive hemodynamic assessment and an acute vasoreactivity test prior to the initiation of advanced therapy.

The acute vasoreactivity test involves administration of a short-acting vasodilator, then measuring the hemodynamic response with a right heart catheter. Agents commonly used include epoprostenol, adenosine, and inhaled nitric oxide. An acute vasoreactivity test is considered positive if mean pulmonary artery pressure decreases at least 10 mmHg and to a value less than 40 mmHg, with an increased or unchanged cardiac output, and a minimally reduced or unchanged systemic blood pressure. Recipients with a positive vasoreactivity test are candidates for a trial of calcium channel blocker therapy. In contrast, recipients with a negative vasoreactivity test should be treated with alternative agents; calcium channel blockers (CCBs) have not shown to be beneficial in these recipients and may be harmful.

Medical Management

Conventional therapies are considered in all patients with PAH regardless of the etiology: diuretics, oxygen therapy, anticoagulants, digoxin, and exercise. Digoxin has been shown to have beneficial effects when used with caution (i.e., patients may be at higher risk for digitalis toxicity and require close monitoring). Patients with a positive vasoreactivity test can be given a trial of CCBs. Patients with a negative vasoreactivity test require advanced therapy with prostacyclin analogues, endothelin receptor antagonists, or phosphodiesterase type 5 (PDE5) inhibitors. Combination advanced therapy has been suggested and is under investigation, but the data are insufficient to draw conclusions. Lung transplantation and combined heart-lung transplantation have been performed in patients refractory to medical management. Objective assessments to measure treatment response include improvement in exercise capacity (6-mile walk test, cardiopulmonary exercise test, treadmill test), hemodynamics, and survival.

The following summarizes the advanced therapies for treatment of PAH (WHO Group 1)

- a. Prostaglandin Analogues
 1. epoprostenol sodium (Flolan[®]) is administered by continuous IV infusion via central venous catheter using an ambulatory infusion pump. FDA approved indications are for long-term treatment of primary pulmonary hypertension and pulmonary hypertension associated with the scleroderma spectrum of disease in NYHA Class III-IV patients who do not respond adequately to conventional therapy.

2. treprostinil sodium (Remodulin[®]) is administered by continuous subcutaneous or intravenous infusion. It is approved for treatment of PAH in patients with NYHA Class II-IV symptoms, to diminish symptoms associated with exercise and in patients who require transition from Flolan, to reduce the rate of clinical deterioration.
 3. iloprost (Ventavis[®]) is delivered by inhalation via nebulizer for treatment of PAH (WHO Group 1) in patients with NYHA Class III-IV symptoms.
- b. Endothelin Receptor Antagonists
1. bosentan (Tracleer[™]) is taken orally for the treatment of PAH (WHO Group 1) in WHO Class III or IV symptoms to improve exercise ability and decrease the rate of clinical worsening.
 2. ambrisentan (LETAIRIS[®]) is taken orally for the treatment of PAH (WHO Group 1) in patients with WHO Class II or III symptoms to improve exercise capacity and delay clinical worsening.
- c. Phosphodiesterase (PDE5) Inhibitors
1. sildenafil citrate (REVATIO[®]) is taken orally for treatment of PAH (WHO Group 1) to improve exercise ability.
 2. tadalafil (CIALIS[®]). No FDA approved indications for PAH or clinical evidence to support use for PAH.
 3. Vardenafil (LEVITRA[®]). No FDA approved indications for PAH or clinical evidence to support use for PAH.

It is important to emphasize the approved treatment for PAH (WHO Group 1) have serious side effects and have NOT shown to be effective in patients with other forms of pulmonary hypertension.

2.0 Eligible Recipients

2.1 General Provisions

To be eligible, NCHC recipients must be enrolled on the date of service.

3.0 When the Procedure, Product, or Service Is Covered

3.1 General Criteria

NCHC covers procedures, products, and services related to this policy when they are medically necessary and

- a. the procedure, product, or service is individualized, specific, and consistent with symptoms or confirmed diagnosis of the illness or injury under treatment, and not in excess of the recipient's needs;
- b. the procedure, product, or service can be safely furnished, and no equally effective and more conservative or less costly treatment is available; **AND**
- c. the procedure, product, or service is furnished in a manner not primarily intended for the convenience of the recipient, the recipient's caretaker, or the provider.

3.2 Specific Criteria

Drug management of primary or secondary pulmonary hypertension is covered under the NC Health Choice Program when it is determined to be medically necessary because the criteria and guidelines shown below are met. The following therapies may be considered medically necessary for the treatment of PAH (WHO Group 1):

- a. epoprostenol sodium (FLOLAN[®]) continuous IV infusion;
- b. treprostinil sodium (REMODULIN[®]) Continuous SC infusion, IV infusion;
- c. Iloprost (VENTAVIS[®]) Inhalation via nebulizer;
- d. bosentan (TRACLEER[®]) oral;
- e. ambrisentan (LETAIRIS[®]) oral;
- f. sildenafil citrate (REVATIO[®]) oral.

3.3 Policy Guidelines

- a. Treatment with epoprostenol requires three steps as follows:
 1. Initial dose-ranging study, which is typically performed as an inpatient. The pulmonary capillary wedge pressure is monitored, the infusion rate of the drug is increased until dose-limiting pharmacologic effects such as nausea, vomiting or headache are elicited. Some practitioners may consider the initial dose-ranging study optional.
 2. Insertion of central venous catheter and attachment to portable infusion pump. Since rebound pulmonary hypertension may recur if the drug is abruptly withdrawn, the drug labeling advises that all recipients should have access to a backup infusion pump and intravenous infusion set.
 3. Ongoing maintenance of portable infusion pump and treatment of complications related to the pump. Complications include catheter thrombosis, sepsis, and pump malfunction. In the clinical trials, a cold pouch and frozen gel packs were used to facilitate extended use at ambient temperatures.
- b. Treatment with iloprost requires the use of a specialized dispensing device.

New York Heart Association (NYHA) Functional Classification for PAH

Class I	Ordinary physical activity does not cause symptoms
Class II	Comfortable at rest, ordinary physical activity causes symptoms
Class III	Comfortable at rest, less than ordinary activity causes symptoms
Class IV	Symptoms at rest

World Health Organization (WHO) Functional Classification for PAH

Class I	No limitation of clinical activity; ordinary physical activity does not cause dyspnea or fatigue
Class II	Slight limitation in physical activity; ordinary physical activity produces dyspnea, fatigue, chest pain, or near-syncope; no symptoms at rest
Class III	Marked limitation of physical activity; less than ordinary physical activity produces dyspnea, fatigue, chest pain, or near-syncope; no symptoms at rest
Class IV	Unable to perform any physical activity without symptoms; dyspnea and/or fatigue present at rest; discomfort increased by any physical activity

4.0 When the Procedure, Product, or Service Is Not Covered

4.1 General Criteria

Procedures, products, and services related to this policy are not covered when

- a. the recipient does not meet the eligibility requirements listed in **Section 2.0**;
- b. the recipient does not meet the medical necessity criteria listed in **Section 3.0**;
- c. the procedure, product, or service unnecessarily duplicates another provider's procedure, product, or service; or
- d. the procedure, product, or service is experimental or investigational.

4.2 Specific Criteria

Pulmonary hypertension drug management is not covered for:

- a. Combination therapy is considered investigational for the treatment of PAH, except when changing from one treatment to another.
- b. The use of epoprostenol, treprostinil, iloprost, bosentan, ambrisentan, or sildenafil is considered investigational for the treatment of non-PAH PH conditions (WHO Groups 2-5), including:
 1. Pulmonary hypertension associated with left heart diseases;
 2. Pulmonary hypertension associated with lung diseases and/ or hypoxemia (including chronic obstructive pulmonary disease);
 3. Pulmonary hypertension due to chronic thrombotic and/or embolic disease;
 4. Miscellaneous group 5 (i.e. sarcoidosis, histiocytosis X and lymphangiomatosis).
- c. The use of tadalafil (CIALIS®) and vardenafil (LEVITRA®) is considered investigational for the treatment of PAH (WHO Group 1) and non-PAH PH conditions (WHO Groups 2-5).

5.0 Requirements for and Limitations on Coverage

5.1 Prior Approval

Prior approval is not required for the drugs or administrative services related to the management of pulmonary hypertension. Prior approval is required to establish medical necessity for skilled nursing visits in the home (to initiate therapy or to monitor progress).

6.0 Providers Eligible to Bill for the Procedure, Product, or Service

To be eligible to bill for procedures, products, and services related to this policy, providers shall

- a. meet NCHC qualifications for participation;
- b. be currently enrolled with NCHC; **AND**
- c. bill only for procedures, products, and services that are within the scope of their clinical practice, as defined by the appropriate licensing entity.

7.0 Additional Requirements

7.1 Compliance

Providers must comply with all applicable federal, state, and local laws and regulations, including the Health Insurance Portability and Accountability Act (HIPAA) and record retention requirements.

8.0 Policy Implementation/Revision Information

Original Effective Date: July 1, 2010

Revision Information:

Date	Section Revised	Change
July 1, 2010		Policy Conversion: Implementation of Session Law 2009-451, Section 10.32 “NC HEALTH CHOICE/PROCEDURES FOR CHANGING MEDICAL POLICY.”

Attachment A: Claims-Related Information

Reimbursement requires compliance with all NCHC guidelines.

A. Claim Type

Professional (CMS-1500/837P transaction)

Institutional (UB-04/837I transaction)

B. Diagnosis Codes

Providers must bill the ICD-9-CM diagnosis codes(s) to the highest level of specificity that supports medical necessity.

C. Procedure Code(s)

HCPCS Codes				
J1325	J3285	K0455	Q4074	S0090
S0155	S9347			

D. Modifiers

Providers are required to follow applicable modifier guidelines.

E. Billing Units

The appropriate procedure code(s) used determines the billing unit(s).

F. Place of Service

Inpatient Hospital (for initial treatment with epoprostenol/FLOLAN[®]) and Home

G. Co-payments

Co-payment(s) may apply to covered prescription drugs and services.

H. Reimbursement

Providers must bill their usual and customary charges.