SPECIALTY GUIDELINE MANAGEMENT

sildenafil tablets (generic)
Revatio (sildenafil tablets and oral suspension)

POLICY

A. INDICATIONS
The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no contraindications or exclusions to the prescribed therapy.

FDA-Approved Indication
Sildenafil/Revatio is indicated for the treatment of pulmonary arterial hypertension (WHO Group I) in adults to improve exercise ability and delay clinical worsening. The delay in clinical worsening was demonstrated when Revatio was added to background epoprostenol therapy.

Studies establishing effectiveness were short-term (12 to 16 weeks), and included predominately patients with New York Heart Association (NYHA) Functional Class II–III symptoms and idiopathic etiology (71%) or associated with connective tissue disease (CTD) (25%).

Limitation of Use: Adding sildenafil to bosentan therapy does not result in any beneficial effect on exercise capacity.

All other indications are considered experimental/investigational and are not a covered benefit.

B. REQUIRED DOCUMENTATION
The following information is necessary to initiate the prior authorization review (where applicable):
- Report with pretreatment results from right heart catheterization

C. EXCLUSIONS
- Treatment with a nitrate/nitric oxide donor medication on a regular or intermittent basis (refer to G.1. Appendix A for examples)
- Concomitant treatment with a guanylate cyclase stimulator (e.g., Adempas)

D. CRITERIA FOR APPROVAL
1. Pulmonary Arterial Hypertension (PAH)
   Authorization of 12 months may be granted when the following criteria are met (a., b., and c. below):
   a. Member has PAH defined as WHO Group 1 class of pulmonary hypertension (refer to G.2. Appendix B).
   b. PAH was confirmed by i. or ii. below:
      i. Pretreatment right heart catheterization with all of the following results:
         - mPAP ≥ 25 mmHg
         - PCWP ≤ 15 mmHg
         - PVR > 3 Wood units
      ii. For infants less than one year of age with any of the following conditions, PAH was confirmed by Doppler echocardiogram if right heart catheterization cannot be performed:
         - Post cardiac surgery
         - Chronic heart disease
         - Chronic lung disease associated with prematurity
         - Congenital diaphragmatic hernia
   c. Member has NYHA functional Class II or III symptoms (refer to G.3. Appendix C) prior to initiation of sildenafil therapy

E. CONTINUATION OF THERAPY
All members (including new members) requesting authorization for continuation of therapy must meet ALL initial authorization criteria.
F. DOSAGE AND ADMINISTRATION
Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines.

1. Dosing Limits
   a. For members who are < 18 years of age: maximum 30 mg per day
   b. For members who are ≥ 18 years of age:
      i. For initial therapy: maximum 60 mg per day
      ii. For continuation of therapy: maximum 240 mg per day for members who have been titrated without adverse effects and experience clinical benefit with higher dose

2. Dosage Forms
   a. For members who are < 18 years of age: authorization may be granted for tablets or suspension
   b. For members who are ≥ 18 years of age: authorization may be granted for tablets only

G. APPENDICES
1. Appendix A: Examples of Nitrate/Nitric Oxide Donor Therapy
   • Isosorbide dinitrate (eg, Isordil)
   • Isosorbide mononitrate (eg, Imdur, Ismo)
   • Nitroglycerin tablets/capsules, patch (eg, Nitro-Dur)
   • Isosorbide dinitrate/hydralazine (BiDil)
   • Amyl nitrate

2. Appendix B: WHO Classification of Pulmonary Hypertension
   WHO Group 1. Pulmonary Arterial Hypertension (PAH)
   1.1 Idiopathic (IPAH)
   1.2 Heritable PAH
      1.2.1 Germline mutations in the bone morphogenetic protein receptor type 2 (BMPR2)
      1.2.2 Activin receptor-like kinase type 1 (ALK1), endoglin (with or without hereditary hemorrhagic telangiectasia), Smad 9, caveolin-1 (CAV1), potassium channel super family K member-3 (KCNK3)
      1.2.3 Unknown
   1.3 Drug- and toxin-induced
   1.4 Associated with:
      1.4.1 Connective tissue diseases
      1.4.2 HIV infection
      1.4.3 Portal hypertension
      1.4.4 Congenital heart diseases
      1.4.5 Schistosomiasis
   1. Pulmonary veno-occlusive disease (PVOD) and/or pulmonary capillary hemangiomatosis (PCH)
   1”. Persistent pulmonary hypertension of the newborn (PPHN)

   WHO Group 2. Pulmonary Hypertension Owing to Left Heart Disease
   2.1 Systolic dysfunction
   2.2 Diastolic dysfunction
   2.3 Valvular disease
   2.4 Congenital/acquired left heart inflow/outflow tract obstruction and congenital cardiomyopathies

   WHO Group 3. Pulmonary Hypertension Owing to Lung Disease and/or Hypoxia
   3.1 Chronic obstructive pulmonary disease
   3.2 Interstitial lung disease
   3.3 Other pulmonary diseases with mixed restrictive and obstructive pattern
   3.4 Sleep-disordered breathing
   3.5 Alveolar hypoventilation disorders
   3.6 Chronic exposure to high altitude
   3.7 Developmental abnormalities

   WHO Group 4. Chronic Thromboembolic Pulmonary Hypertension (CTEPH)
WHO Group 5. Pulmonary Hypertension with Unclear Multifactorial Mechanisms
5.1 Hematologic disorders: Chronic hemolytic anemia, myeloproliferative disorders, splenectomy
5.2 Systemic disorders: sarcoidosis, pulmonary Langerhans cell histiocytosis: lymphangioleiomyomatosis, neurofibromatosis, vasculitis
5.3 Metabolic disorders: glycogen storage disease, Gaucher disease, thyroid disorders
5.4 Others: tumoral obstruction, fibrosing mediastinitis, chronic renal failure on dialysis, segmental PH

3. Appendix C: New York Heart Association Functional Classification

- **Class I**: Patients with pulmonary hypertension 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 pulmonary hypertension 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 pulmonary hypertension 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 pulmonary hypertension with inability to carry out any physical activity without symptoms. These patients manifest signs of right heart failure. Dyspnea and/or fatigue may be present even at rest. Discomfort is increased by any physical activity.

REFERENCES