Clinical Policy: Sildenafil (Revatio)

Reference Number: CP.PHAR.197
Effective Date: 03/16
Last Review Date: 03/17

Coding Implications
Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description
The intent of the criteria is to ensure that patients follow selection elements established by Centene® clinical policy for sildenafil (Revatio®)*.

**Revatio and its generic, sildenafil, should not be confused with the brand formulation of sildenafil, Viagra.*

Policy/Criteria
It is the policy of health plans affiliated with Centene Corporation® that Revatio is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Pulmonary Hypertension (must meet all):

1. Prescribed by or in consultation with a cardiologist or pulmonologist experienced in the diagnosis and treatment of pulmonary hypertension (PH);
2. Diagnosis of PH confirmed by right heart catheterization and classified as (a and b):
   a. WHO Group 1: PAH (pulmonary arterial hypertension; Appendix B) and (i or ii):
      i. Inadequate response or contraindication to acute vasodilator testing;
      ii. Trial and failure of, or contraindication to, at least one calcium channel blocker;
   b. WHO/NYHA Functional Class II, III or IV (Appendix C);
3. Prescribed dose of Revatio does not exceed 60 mg/day (oral formulations) or 30 mg/day (intravenous formulations) in divided doses.

Approval duration: 6 months

B. Other diagnoses/indications: Refer to CP.PHAR.57 - Global Biopharm Policy.

II. Continued Approval

A. Pulmonary Hypertension (must meet all)**:**

1. Currently receiving medication via Centene benefit or member has previously met all initial approval criteria;
2. Member is responding positively to therapy;
3. Prescribed dose of Revatio does not exceed 20 mg (oral formulations) or 10 mg (intravenous formulations) three times daily.

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy;
2. Refer to CP.PHAR.57 - Global Biopharm Policy.

Background

Description/Mechanism of Action:

Revatio, a PDE-5 inhibitor, is the citrate salt of sildenafil, a selective inhibitor of cyclic guanosine monophosphate (cGMP)-specific PDE-5. Sildenafil is also marketed as Viagra for erectile dysfunction. Sildenafil is an inhibitor of cGMP specific PDE-5 in the smooth muscle of the pulmonary vasculature, where PDE-5 is responsible for degradation of cGMP. Sildenafil, therefore, increases cGMP within pulmonary vascular smooth muscle cells resulting in relaxation. In patients with PAH, this can lead to vasodilation of the pulmonary vascular bed and, to a lesser degree, vasodilatation in the systemic circulation.

Formulations:

Intravenous solution:
Revatio: 10 mg/12.5 mL (12.5 mL)
Generic: 10 mg/12.5 mL (12.5 mL)
Reconstituted oral suspension:
Revatio: 10 mg/mL (112 mL)
Oral tablet:
Revatio: 20 mg
Generic: 20 mg

FDA Approved Indications:

Revatio is a PDE-5 inhibitor/tablet (generic available), oral suspension (generic unavailable), or intravenous bolus injection (generic available) indicated for:

- Treatment of PAH (WHO Group 1) 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 and included predominately patients with NYHA Functional Class II-III symptoms and idiopathic etiology or associated with connective tissue disease.

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

Appendices

Appendix A: Abbreviation Key

- FC: functional classification
- NYHA: New York Heart Association
- PAH: pulmonary arterial hypertension
- PH: pulmonary hypertension
- WHO: World Health Organization

Appendix B: Pulmonary Hypertension: WHO Classification

- Group 1: PAH (pulmonary arterial hypertension)
- Group 2: PH due to left heart disease
- Group 3: PH due to lung disease and/or hypoxemia

- Group 4: CTEPH (chronic thromboembolic pulmonary hypertension)
- Group 5: PH due to unclear multifactorial mechanisms

Appendix C: Pulmonary Hypertension: WHO/NYHA Functional Classes (FC)

Treatment Approach*	FC	Status at Rest	Tolerance of Physical Activity (PA)	PA Limitations	Heart Failure
Monitoring for progression of PH and treatment of co-existing conditions	I	Comfortable at rest	No limitation	Ordinary PA does not cause undue dyspnea or fatigue, chest pain, or near syncope.	
Advanced treatment of PH with PH-targeted therapy - see Appendix D**	II	Comfortable at rest	Slight limitation	Ordinary PA causes undue dyspnea or fatigue, chest pain, or near syncope.	
	III	Comfortable at rest	Marked limitation	Less than ordinary PA causes undue dyspnea or fatigue, chest pain, or near syncope.	
	IV	Dyspnea or fatigue may be present at rest	Inability to carry out any PA without symptoms	Discomfort is increased by any PA.	Signs of right heart failure

*PH supportive measures may include diuretics, oxygen therapy, anticoagulation, digoxin, exercise, pneumococcal vaccination. **Advanced treatment options also include calcium channel blockers.

Appendix D: Pulmonary Hypertension: Targeted Therapies

Mechanism of Action	Drug Class	Drug Subclass	Drug	Brand/Generic Formulations
Reduction of pulmonary arterial pressure through vasodilation	Prostacyclin* pathway agonist **Member of the prostanoid class of fatty acid derivatives.*	Prostacyclin	Epoprostenol	Veletri (IV) Flolan (IV) Flolan generic (IV)
		Synthetic prostacyclin analog	Treprostinil	Orenitram (oral tablet) Remodulin (IV) Tyvasco (inhalation)
			Iloprost	Ventavis (inhalation)
		Non-prostanoid prostacyclin receptor (IP receptor) agonist	Selexipag	Uptravi (oral tablet)
	Endothelin receptor antagonist	Selective receptor antagonist	Ambrisentan	Letairis (oral tablet)
		Nonselective dual action receptor antagonist	Bosentan	Tracleer (oral tablet)
			Macitentan	Opsummit (oral tablet)

Mechanism of Action	Drug Class	Drug Subclass	Drug	Brand/Generic Formulations
	Nitric oxide-cyclic guanosine monophosphate enhancer	Phosphodiesterase type 5 (PDE5) inhibitor	Sildenafil	Revatio (IV, oral tablet, oral suspension)
			Tadalafil	Adcirca (oral tablet)
		Guanylate cyclase stimulant	Riociguat	Adempas (oral tablet)

Coding Implications
Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
N/A	

Reviews, Revisions, and Approvals	Date	Approval Date
Policy split from CP.PHAR.33.PAH and converted to new template. Criteria: added specialist requirement; removed echocardiogram as an option for confirming a PH diagnosis; removed hard stop after 3 months of therapy. Appendices removed: 1) examples of calcium channel blocker contraindications; 2) nitrate therapy examples; 3) PAH definition.	02/16	03/16
FC II added to the prostanoid class of PH drugs. Safety criteria were removed unless they 1) represent contraindications or black box warnings not covered by a REMS program, and 2) provide specific lab/imaging parameters that must be met prior to initiation of therapy. An efficacy statement is added to the continuation criteria. Initial and continuation durations increased to 6 and 12 months respectively. Appendices covering PH groups, functional class and therapies reorganized.	02/17	03/17

References
1. Revatio prescribing information. New York, NY: Pfizer Inc.; April 2015. Available at http://labeling.pfizer.com/ShowLabeling.aspx?id=645. Accessed February 10, 2017.
2. McLaughlin VV, Archer SL, Badesch DB, et al. ACCF/AHA 2009 expert consensus document on pulmonary hypertension: A report of the American College of Cardiology Foundation Task Force on Expert Consensus Documents and the American Heart Association - developed in collaboration with the American College of Chest Physicians, American Thoracic Society, Inc., and the Pulmonary Hypertension Association. *J Am Coll Cardiol.* 2009; 53(17): 1573-1619.
3. Taichman D, Ornelas J, Chung L, et. al. CHEST guideline and expert panel report:

Pharmacologic therapy for pulmonary arterial hypertension in adults. *Chest.* 2014; 146 (2): 449-475.
4. Abman SH, Hansmann G, Archer SL, et al. Pediatric pulmonary hypertension: Guidelines from the American Heart Association and American Thoracic Society. *Circulation.* 2015 Nov 24; 132(21): 2037-99.
5. Kim NH, Delcroix M, Jenkins DP, et al. Chronic thromboembolic pulmonary hypertension. *J Am Coll Cardiol* 2013; 62(25): Suppl D92-99.
6. Rubin LJ and Hopkins W. Overview of pulmonary hypertension in adults. In: UpToDate, Waltham, MA: Walters Kluwer Health; 2017. Available at UpToDate.com. Accessed February 14, 2017.
7. Rubin LJ and Hopkins W. Clinical features and diagnosis of pulmonary hypertension in adults. In: UpToDate, Waltham, MA: Walters Kluwer Health; 2017. Available at UpToDate.com. Accessed February 14, 2017.
8. Hopkins W and Rubin LJ. Treatment of pulmonary hypertension in adults. In: UpToDate, Waltham, MA: Walters Kluwer Health; 2017. Available at UpToDate.com. Accessed February 14, 2017.
9. Fedullo PF. Clnical manifestations and diagnosis of chronic thromboembolic pulmonary hypertension. In: UpToDate, Waltham, MA: Walters Kluwer Health; 2017. Available at UpToDate.com. Accessed February 14, 2017.
10. Fedullo PF. Overview of the treatment of chronic thromboembolic pulmonary hypertension. In: UpToDate, Waltham, MA: Walters Kluwer Health; 2017. Available at UpToDate.com. Accessed February 14, 2017.
11. Fedullo PF. Chronic thromboembolic pulmonary hypertension: Surgical treatment. In: UpToDate, Waltham, MA: Walters Kluwer Health; 2017. Available at UpToDate.com. Accessed February 14, 2017.
12. Fedullo PF. Chronic thromboembolic pulmonary hypertension: Medical treatment. In: UpToDate, Waltham, MA: Walters Kluwer Health; 2017. Available at UpToDate.com. Accessed February 14, 2017.
13. Nazzareno G, Humbert M, Vachiary JL, et al. 2015 ESC/ERS Guidelines for the diagnosis and treatment of Pulmonary Hypertension. European Heart Journal. Doi:10.1093/eurheartj/ehv317.

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

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This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

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Note: For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

Note: For Medicare members, to ensure consistency with the Medicare National Coverage Determinations (NCD) and Local Coverage Determinations (LCD), all applicable NCDs, LCDs, or Medicare coverage articles should be reviewed prior to applying the criteria set forth in this clinical policy. Refer to the CMS website at http://www.cms.gov for additional information.