

Sildenafil (Revatio®)

Issued by PHA's Scientific Leadership Council

Information is based on the United States Food and Drug Administration drug labeling

Last Updated November 2013

WHAT IS SILDENAFIL?

Sildenafil is an oral medication called a phosphodiesterase-5 (PDE5) inhibitor approved for the treatment of pulmonary arterial hypertension (PAH) in World Health Organization (WHO) Group 1 patients. The goal of this therapy is to improve exercise ability and delay clinical worsening. Research studies showing the effectiveness of the medication included mostly patients with symptoms that were rated as WHO Functional Class II-III.

Sildenafil is marketed as Revatio® for PAH and was approved by the United States Food and Drug Administration (FDA) in 2005. Sildenafil is also marketed as Viagra® which is FDA-approved for the treatment of erectile dysfunction but not for the treatment of PAH.

HOW DOES SILDENAFIL WORK?

PDE5 is a substance produced in the lungs and other parts of the body that breaks down another substance called cyclic guanosine monophosphate (GMP). Cyclic GMP causes the blood vessels (arteries) to relax and widen. Sildenafil decreases the activity of PDE5, so that more cyclic GMP is available for the blood vessels inside the lungs. This leads to relaxation, or widening, of those vessels. Relaxing and widening of the blood vessels in the lungs decreases the pulmonary blood pressure to the heart and improves its function. This reduces blood pressure in the lungs which generally results in the ability to be more active. Research studies have verified this improvement.

HOW IS SILDENAFIL SUPPLIED?

Revatio® is only available as a round, white 20 mg pill, to distinguish it from Viagra®, which is a blue diamond-shaped pill.

Revatio® injection is supplied as a single-use vial containing 10 mg (12.5 mL) of sildenafil.

HOW CAN A PATIENT OBTAIN SILDENAFIL?

Sildenafil must be prescribed by a physician, and insurance approval must be obtained prior to starting therapy. It is carried by most retail and specialty pharmacies, including Accredo Health Inc., Aetna Specialty Pharmacy, CVS Caremark, Cigna Tel-Drug, CuraScript, Kaiser Permanente Specialty Pharmacy, Precision Rx, Walgreens Specialty Pharmacy (Medmark) and WellCare.

WILL INSURANCE PAY FOR SILDENAFIL?

It is expected that most insurance plans will pay for sildenafil prescriptions; however, plans with a set co-payment may result in additional cost to the patient.

Medicaid and most state-run insurance plans will pay for sildenafil. Medicare will also cover sildenafil in most cases under Medicare Part D.

Pfizer RSVP Program, 1-888-327-7787, offers a variety of options to cover the cost of the co-payment for any for any patient proving evidence of adequate financial need. Caring Voice Coalition (888-267-1440), an organization that provides grants to assist with drug cost for

Sildenafil (Revatio®)

Continued

patients with chronic illnesses, may also provide coverage if the patient proves a need for such assistance.

WILL INSURANCE PAY FOR SILDENAFIL?

It is expected that most health insurance plans will pay part of the cost of this medication. However, some plans still leave patients with a high out-of-pocket responsibility.

Depending on your insurance type, you may be eligible for assistance from the company that manufactures your therapy or from a non-profit charitable assistance organization. For more information visit www.PHAssociation.org/Help or call 301-565-3004.

WHAT ARE THE FREQUENT SIDE EFFECTS OF SILDENAFIL?

Sildenafil is generally well tolerated. The most frequent side effects are:

- Nose bleeds
- Headache
- Upset stomach and heartburn
- Flushing of the skin
- Difficulty sleeping
- Worsening shortness of breath
- Nasal congestion.

Other side effects include:

- Fluid retention
- Nausea and diarrhea
- Pain in the extremity (arm or leg)
- Temporary muscle aches
- Fever
- Numbness

A reduction in blood pressure throughout the body may occur because sildenafil relaxes blood vessels (arteries) throughout the body. Caution must be used in patients with low blood pressure, less than 90/50 mmHg for example. Caution is also needed in patients with dehydration, left-sided heart diseases and certain abnormalities of the body's nervous system function.

Taking certain medications such as nitrates, nitric oxide donors or alpha blockers along with sildenafil can cause a significant drop in blood pressure. This could result in loss of consciousness or even death. You should make certain that you are not taking these medications

Sildenafil (Revatio®)

Continued

before starting sildenafil. Use of sildenafil with medications known as nitrates is **CONTRAINDICATED**.

Prolonged erection (greater than four hours) in a male patient is a rare but very serious side effect; if this should happen to you, you should go to an emergency room or contact your doctor immediately.

Sudden loss of vision in one or both eyes has occurred in patients on PDE5 inhibitors. Such an event may represent serious dysfunction of the optic nerve and requires immediate medical attention.

Sudden loss of hearing may occur and may be accompanied by dizziness and/or ear ringing. Patients should seek prompt medical attention should this occur.

HOW ARE SIDE EFFECTS OF SILDENAFIL MONITORED?

No regular bloodwork for side effects is required.

Your doctor may ask you to monitor your blood pressure on a regular basis particularly during your first few days on treatment or with a dose increase. Blood pressure monitoring is not needed for most patients.

If you experience any of the symptoms mentioned in the previous section, you should promptly notify your physician.

WHAT ARE CONSIDERATIONS FOR USE OF SILDENAFIL IN SPECIAL POPULATIONS?

The safety and effectiveness of sildenafil in pediatric PAH patients has not been established.

Sildenafil does not exhibit harm to the fetus in animal studies; however it has not been evaluated in pregnant women or women who are breastfeeding. It should be used in pregnant or nursing mothers only if the potential benefit justifies the risk to the fetus or infant.

Safety and efficacy in pediatric patients has not been established, and this drug should not be used in patients under 18 years of age.

Mild-to-moderate liver disease does not require a dose adjustment. Severe liver disease has not been studied.

No dose adjustment is required in patients with kidney disease.

Sildenafil may be associated with a serious condition known as vaso-occlusive crisis in patients with PH and sickle cell disease. The effectiveness of sildenafil in PH secondary to sickle cell anemia has not been established.

Sildenafil is not recommended in patients with either of two rare diseases often associated with PAH: pulmonary veno-occlusive disease and pulmonary capillary hemangiomatosis.

Sildenafil (Revatio®)

Continued

COULD A PATIENT BE ALLERGIC TO SILDENAFIL?

This is possible, but not likely.

WHAT ARE IMPORTANT DRUG INTERACTIONS WITH SILDENAFIL? (PLEASE SEE PACKAGE INSERT FOR FULL DETAILS)

Sildenafil should not be used in combination with nitrates or nitric oxide donors as an unsafe drop in systemic blood pressure may occur.

Caution should be used if sildenafil is to be used in combination with either alcohol or anti-hypertension or blood-pressure-lowering medications.

Sildenafil is broken down predominantly by an enzyme called CYP3A in the liver; therefore, important interactions may occur with medications that affect this enzyme pathway.

Simultaneous use of bosentan and sildenafil may result in increased bosentan blood levels and decreased sildenafil blood levels. It is not known if these changes are clinically significant. Although a drug interaction has been demonstrated with sildenafil and bosentan, dose adjustments are presently not recommended for either drug.

Patients with human immunodeficiency virus (HIV or AIDS) who are taking medicines called antiretroviral agents should not use a phosphodiesterase inhibitor such as sildenafil since it can dramatically impair the efficacy of the antiretroviral.

Use of sildenafil with epoprostenol may reduce the blood level of sildenafil.

Use of sildenafil with beta blockers (another type of heart or blood pressure medicine) may increase the levels of sildenafil.

MISCELLANEOUS CONSIDERATIONS:

IS THERE ANY RISK OF BLINDNESS WHEN USING SILDENAFIL?

There have been rare reports of blindness with use of all the currently available PDE5 inhibitors, including sildenafil. This type of blindness, which may be permanent, is called non-arteritic anterior ischemic optic neuropathy (NAION). It is not yet clear whether this is related to the use of sildenafil or to the underlying cardiovascular diseases that place the persons at risk for this particular type of blindness, even in the absence of sildenafil use.

There is no research to determine whether use of sildenafil is beneficial or safe in patients with retinitis pigmentosa, and use in these patients is not recommended.

As noted above, patients taking sildenafil should seek immediate medical attention in the event of sudden vision loss.

CAN MEN AND WOMEN TAKE SILDENAFIL?

Yes, studies have evaluated sildenafil in both men and women with PAH, and no differences in side effects have been reported between genders. Studies have not shown any effect on sexual function in women who have taken sildenafil.