HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use REVATIO safely and effectively. See full prescribing information for REVATIO.

REVATIO (sildenafil) tablets, for oral use
REVATIO (sildenafil) for oral suspension
REVATIO (sildenafil) injection, for intravenous use
Initial U.S. Approval: 1998

----------RECENT MAJOR CHANGES----------

Indication and Use (1)	08/2012
Dosage and Administration (2.3)	08/2012
Contraindications (4)	08/2012
Warnings and Precautions (5)	08/2012

----------INDICATIONS AND USAGE----------

REVATIO is a phosphodiesterase-5 (PDE-5) inhibitor indicated for the treatment of pulmonary arterial hypertension (PAH) (WHO Group I) in adults to improve exercise ability and delay clinical worsening. Studies establishing effectiveness were short-term (12 to 16 weeks), and included predominately patients with NYHA Functional Class II-III symptoms. Etiologies were idiopathic (71%) or associated with connective tissue disease (25%). (1)

Limitation of Use: The efficacy of REVATIO has not been adequately evaluated in patients taking bosentan concurrently. (1)

----------DOSAGE AND ADMINISTRATION----------

Tablet and oral suspension: 20 mg three times a day, 4-6 hours apart (2.1)
Injection: 10 mg (12.5 mL) three times a day administered as an intravenous bolus injection (2.2)

----------DOSAGE FORMS AND STRENGTHS----------

- *Tablets*: 20 mg (3)
- *Injection*: 10 mg (12.5 mL) single use vial (3)
- *For Oral Suspension*: 10 mg/mL (3)

----------CONTRAINDICATIONS----------

- Use with organic nitrates (4)
- History of hypersensitivity reaction to sildenafil or any component of the tablet, injection, or oral suspension (4)

----------WARNINGS AND PRECAUTIONS----------

- Increased mortality with increasing doses in pediatric patients. Not recommended for use in pediatric patients. (5.1)
- Vasodilation effects may be more common in patients with hypotension or on antihypertensive therapy. (5.2)
- Use in pulmonary veno-occlusive disease may cause pulmonary edema and is not recommended. (5.3)
- Hearing or visual impairment: Seek medical attention if sudden decrease or loss of vision or hearing occurs. (5.5, 5.6)
- Pulmonary hypertension secondary to sickle cell disease: REVATIO may cause serious vaso-occlusive crises. (5.9)

----------ADVERSE REACTIONS----------

Most common adverse reactions greater than or equal to 3% and more frequent than placebo were epistaxis, headache, dyspepsia, flushing, insomnia, erythema, dyspnea, and rhinitis. (6.1, 6.2)

To report SUSPECTED ADVERSE REACTIONS, contact Pfizer at 1-800-438-1985 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

----------DRUG INTERACTIONS----------

- Concomitant alpha-blockers or amlodipine: Note additive blood pressure lowering effects. (7)
- Use with ritonavir and other potent CYP3A inhibitors: Not recommended. (7, 12.3)
- Concomitant PDE-5 inhibitors: Avoid use with Viagra or other PDE-5 inhibitors. (5.7)

See 17 for PATIENT COUNSELING INFORMATION AND FDA-approved patient labeling

Revised: August 2012

FULL PRESCRIBING INFORMATION: CONTENTS*

*Sections or subsections omitted from the Full Prescribing Information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

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 *[see Clinical Studies (14)]*.

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

The efficacy of REVATIO in the treatment of pulmonary arterial hypertension (PAH) has not been adequately evaluated in patients taking bosentan.

2 DOSAGE AND ADMINISTRATION

2.1 REVATIO Tablets and Oral Suspension

The recommended dose of REVATIO is 20 mg three times a day (TID). Administer REVATIO doses 4-6 hours apart.

In the clinical trial no greater efficacy was achieved with the use of higher doses. Treatment with doses higher than 20 mg TID is not recommended.

2.2 REVATIO Injection

REVATIO injection is for the continued treatment of patients with PAH who are currently prescribed oral REVATIO and who are temporarily unable to take oral medication.

The recommended dose is 10 mg (12.5 mL) administered as an intravenous bolus injection three times a day (TID). The dose of REVATIO injection does not need to be adjusted for body weight.

A 10 mg dose of REVATIO injection is predicted to provide pharmacological effect of sildenafil and its N-desmethyl metabolite equivalent to that of a 20 mg oral dose.

2.3 Reconstitution of the Powder for Oral Suspension

1. Tap the bottle to release the powder.
2. Remove the cap.
3. Accurately measure out 60 mL of water and pour the water into the bottle. (Figure 1)

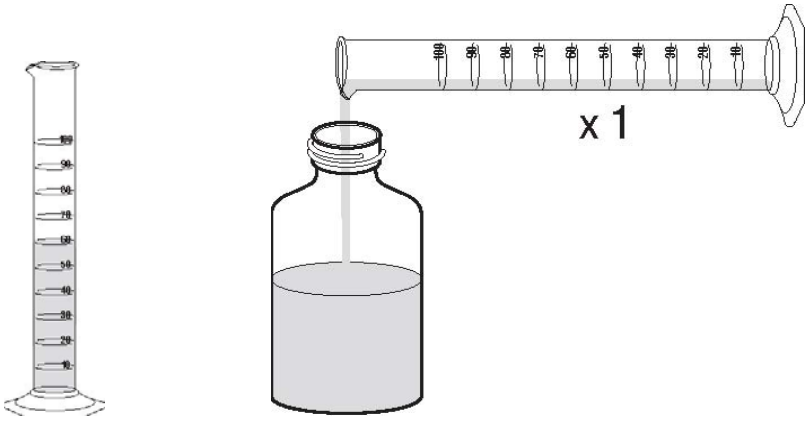

Figure 1

4. Replace the cap and shake the bottle vigorously for a minimum of 30 seconds. (Figure 2)

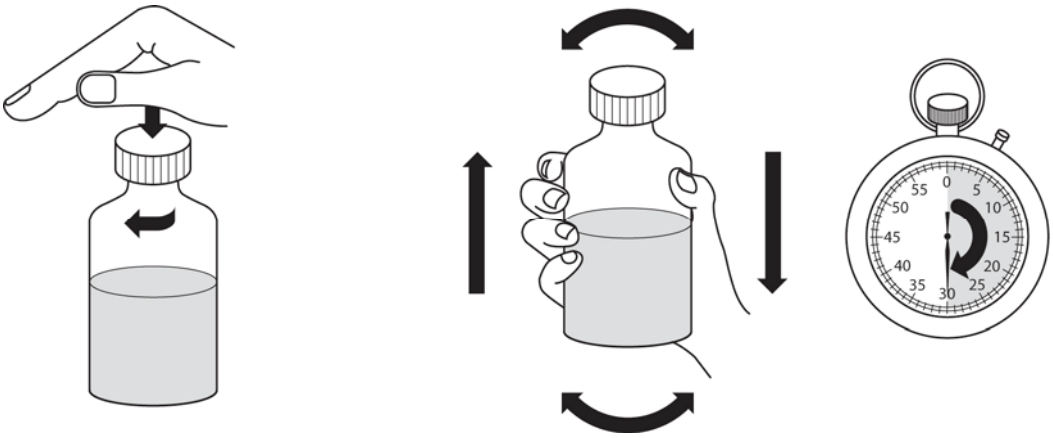

Figure 2

5. Remove the cap.
6. Accurately measure out another 30 mL of water and add this to the bottle. You should always add a total of 90 mL of water irrespective of the dose prescribed. (Figure 3)

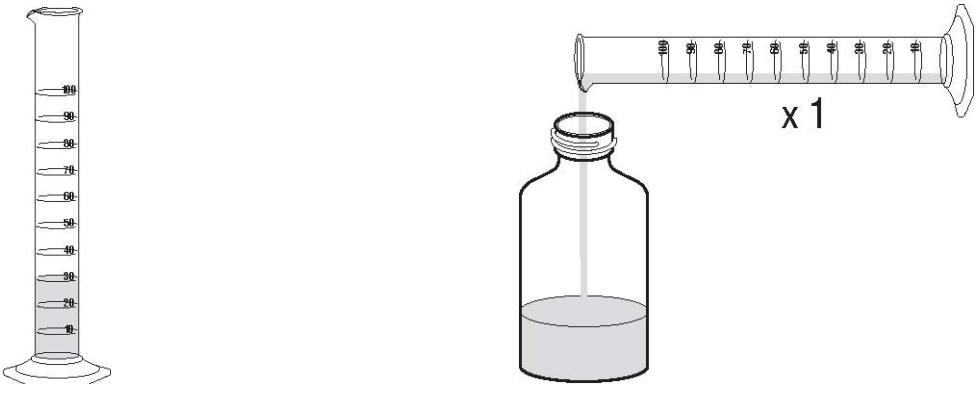

Figure 3

7. Replace the cap and shake the bottle vigorously for a minimum of 30 seconds. (Figure 4)

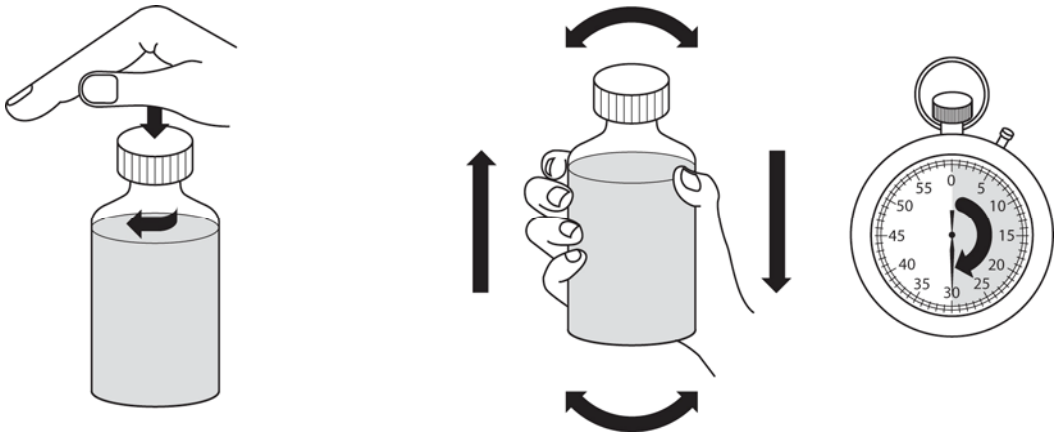

Figure 4

8. Remove the cap.
9. Press the bottle adaptor into the neck of the bottle (as shown on Figure 5, below). The adaptor is provided so that you can fill the oral syringe with medicine from the bottle. Replace the cap on the bottle.

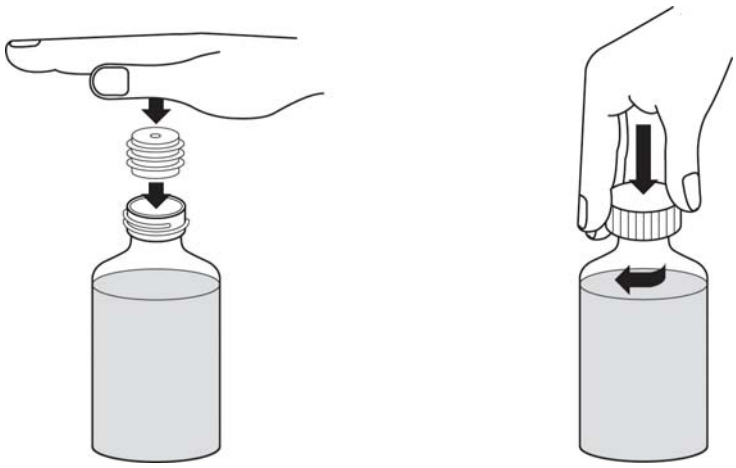

Figure 5

10. Write the expiration date of the constituted oral suspension on the bottle label (the expiration date of the constituted oral suspension is 30 days from the date of constitution).

Incompatibilities
Do not mix with any other medication or additional flavoring agent.

3 DOSAGE FORMS AND STRENGTHS

REVATIO Tablets
REVATIO tablets are supplied as white, film-coated, round tablets engraved with “RVT20” containing sildenafil citrate equivalent to 20 mg of sildenafil.

REVATIO Injection
REVATIO injection is supplied as a single use vial containing 10 mg (12.5 mL) of sildenafil.

REVATIO for Oral Suspension
REVATIO for oral suspension is supplied in 125 mL bottles containing 32.27 g of a white to off-white powder. Following constitution with water, the volume of the oral suspension is 112 mL and each bottle contains 1.57 g of sildenafil citrate (1.12 g sildenafil). A 2 mL oral syringe and a press-in bottle adaptor are also provided.

4 CONTRAINDICATIONS

REVATIO is contraindicated in patients with:

- Concomitant use of organic nitrates in any form, either regularly or intermittently, because of the greater risk of hypotension *[see Warnings and Precautions (5.2)]*.

- Known hypersensitivity to sildenafil or any component of the tablet, injection, or oral suspension. Hypersensitivity, including anaphylactic reaction, anaphylactic shock and anaphylactoid reaction, has been reported in association with the use of sildenafil.

5 WARNINGS AND PRECAUTIONS

5.1 Mortality with Pediatric Use

In a long-term trial in pediatric patients with PAH, an increase in mortality with increasing REVATIO dose was observed. Deaths were first observed after about 1 year and causes of death were typical of patients with PAH. Use of REVATIO, particularly chronic use, is not recommended in children. *[see Use in Specific Populations (8.4)]*.

5.2 Hypotension

REVATIO has vasodilatory properties, resulting in mild and transient decreases in blood pressure. Before prescribing REVATIO, carefully consider whether patients with certain underlying conditions could be adversely affected by such vasodilatory effects (e.g., patients on antihypertensive therapy or with resting hypotension [BP less than 90/50], fluid depletion, severe left ventricular outflow obstruction, or autonomic dysfunction). Monitor blood pressure when co-administering blood pressure lowering drugs with REVATIO.

5.3 Worsening Pulmonary Vascular Occlusive Disease

Pulmonary vasodilators may significantly worsen the cardiovascular status of patients with pulmonary veno-occlusive disease (PVOD). Since there are no clinical data on administration of REVATIO to patients with veno-occlusive disease, administration of REVATIO to such patients is not recommended. Should signs of pulmonary edema occur when REVATIO is administered, consider the possibility of associated PVOD.

5.4 Epistaxis

The incidence of epistaxis was 13% in patients taking REVATIO with PAH secondary to CTD. This effect was not seen in idiopathic PAH (REVATIO 3%, placebo 2%) patients. The incidence of epistaxis was also higher in REVATIO-treated patients with a concomitant oral vitamin K antagonist (9% versus 2% in those not treated with concomitant vitamin K antagonist).

The safety of REVATIO is unknown in patients with bleeding disorders or active peptic ulceration.

5.5 Visual Loss

When used to treat erectile dysfunction, non-arteritic anterior ischemic optic neuropathy (NAION), a cause of decreased vision including permanent loss of vision, has been reported postmarketing in temporal association with the use of phosphodiesterase type 5 (PDE-5) inhibitors, including sildenafil. Most, but not all, of these patients had underlying anatomic or vascular risk factors for developing NAION, including but not necessarily limited to: low cup to disc ratio (“crowded disc”), age over 50, diabetes, hypertension, coronary artery disease, hyperlipidemia and smoking. It is not possible to determine whether these events are related directly to the use of PDE-5 inhibitors, to the patient’s underlying vascular risk factors or anatomical defects, to a combination of these factors, or to other factors.

Advise patients to seek immediate medical attention in the event of a sudden loss of vision in one or both eyes while taking PDE-5 inhibitors, including REVATIO. Physicians should also discuss the increased risk of NAION with patients who have already experienced NAION in one eye, including whether such individuals could be adversely affected by use of vasodilators, such as PDE-5 inhibitors.

There are no controlled clinical data on the safety or efficacy of REVATIO in patients with retinitis pigmentosa, a minority whom have genetic disorders of retinal phosphodiesterases. Prescribe REVATIO with caution in these

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