



NDA 21-845/S-001

Pfizer Inc.
Attention: Mr. Robert Clark
235 East 42nd Street
New York, NY 10017

Dear Mr. Clark:

Please refer to your supplemental new drug application dated July 25, 2005 under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Revatio (sildenafil citrate) 20 mg Tablets.

We acknowledge receipt of your submission dated August 9, 2005.

This "Changes Being Effected in 30 days" supplemental new drug application provides for the following changes to the approved labeling:

1. The following sentence was added to the **DESCRIPTION** section, as the last sentence of the first paragraph:

Sildenafil is also marketed as VIAGRA[®] for male erectile dysfunction.

2. In the **CLINICAL PHARMACOLOGY/Pharmacodynamics** section, the third paragraph has been changed from:

After chronic dosing of 80 mg t.i.d. sildenafil to healthy patients, the largest mean change from baseline in supine systolic and supine diastolic blood pressures was a decrease of 9.0 mmHg and 8.4 mmHg, respectively.

To:

After chronic dosing of 80 mg t.i.d. sildenafil to healthy volunteers, the largest mean change from baseline in supine systolic and supine diastolic blood pressures was a decrease of 9.0 mmHg and 8.4 mmHg, respectively.

3. The following paragraphs were added at the end of the **PRECAUTIONS/Information for Patients** section:

Sildenafil is also marketed as VIAGRA[®] for male erectile dysfunction.

Physicians should advise patients to seek immediate medical attention in the event of a sudden loss of vision in one or both eyes while taking all PDE5 inhibitors, including REVATIO. Such an event may be a sign of non-arteritic anterior ischemic optic neuropathy (NAION), a cause of decreased vision including permanent loss of vision, that has been reported rarely post-marketing in temporal association with the use of all PDE5 inhibitors when used in the treatment of male-erectile dysfunction. It is not possible to determine whether these events are related directly to the use of PDE5 inhibitors or to other factors. Physicians should also discuss with patients the increased risk of NAION in individuals who

have already experienced NAION in one eye, including whether such individuals could be adversely affected by use of vasodilators, such as PDE5 inhibitors (see **ADVERSE REACTIONS**).

4. The following paragraph was added at the end of the **ADVERSE REACTIONS** section:

When used to treat male-erectile dysfunction, non-arteritic anterior ischemic optic neuropathy (NAION), a cause of decreased vision including permanent loss of vision, has been reported rarely post-marketing in temporal association with the use of phosphodiesterase type 5 (PDE5) inhibitors, including sildenafil citrate. 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 PDE5 inhibitors, to the patient’s underlying vascular risk factors or anatomical defects, to a combination of these factors, or to other factors (see **PRECAUTIONS/Information for Patients**).

The following additional changes were noted in the proposed labeling:

1. The heading was changed from:

REVATIO™
(sildenafil citrate) Tablets, 20 mg

Rx Only

To:

REVATIO™
(sildenafil citrate) Tablets

2. The end of the label was changed from:

Distributed by
 **U.S. Pharmaceuticals**
Pfizer Inc, NY, NY 10017

LAB-0313-1

June 2005

© 2005 Pfizer Inc

To:

 **Pfizer Labs**
Division of Pfizer Inc, NY, NY 10017

Rx Only

LAB-0313-4

Issued July 2005

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We have completed our review of this application, as amended. This application is approved, effective on the date of this letter, for use as recommended in the agreed-upon labeling text.

The final printed labeling (FPL) must be identical to the submitted labeling (package insert included in your submission of July 25, 2005).

The electronic labeling rule published December 11, 2003, (68 FR 69009) requires submission of labeling content in electronic format effective June 8, 2004. For additional information, consult the following guidances for industry regarding electronic submissions: *Providing Regulatory Submissions in Electronic Format - NDAs* (January 1999) and *Providing Regulatory Submissions in Electronic Format – Content of Labeling* (February 2004). The guidances specify that labeling be submitted in *pdf* format. To assist in our review, we request that labeling also be submitted in MS Word format. If formatted copies of all labeling pieces (i.e., package insert, patient package insert, container labels, and carton labels) are submitted electronically, labeling does not need to be submitted in paper.

If you issue a letter communicating important information about this drug product (i.e., a “Dear Health Care Professional” letter), we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH, HFD-410
FDA
5600 Fishers Lane
Rockville, MD 20857

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, please call Melissa Robb, Regulatory Health Project Manager, at (301) 796-1138.

Sincerely,

{See appended electronic signature page}

Norman Stockbridge, M.D., Ph.D.
Acting Director
Division of Cardiovascular and Renal Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

**This is a representation of an electronic record that was signed electronically and
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/s/

Norman Stockbridge
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