



NDA 21-845/S-004

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 November 1, 2007, under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Revatio (sildenafil citrate) 20 mg Tablets.

This supplemental new drug application provides for changes to the approved package insert as follows:

- 1) To add the following paragraph to the **PRECAUTIONS, Information for Patients** section of the package insert:

Physicians should advise patients to seek prompt medical attention in the event of sudden decrease or loss of hearing while taking all PDE5 inhibitors, including REVATIO. These events, which may be accompanied by tinnitus and dizziness, have been reported in temporal association to the intake of PDE5 inhibitors, including REVATIO. It is not possible to determine whether these events are related directly to the use of PDE5 inhibitors or to other factors (see **ADVERSE REACTIONS, Clinical Trials and Post-Marketing Experience**).

- 2) To add the section header "**Clinical Trials**" under the **ADVERSE REACTIONS** section of the package insert.

- 3) To add the section header "**Post-Marketing Experience**" under the **ADVERSE REACTIONS** section of the package insert.

- 4) To add the following text to the **ADVERSE REACTIONS, Post-Marketing Experience** section of the package insert:

"Cases of sudden decrease or loss of hearing have been reported post-marketing in temporal association with the use of PDE5 inhibitors, including REVATIO. In some of the cases, medical conditions and other factors were reported that may have also played a role in the otologic adverse events. In many cases, medical follow-up information was limited. It is not possible to determine whether these reported events are related directly to the use of REVATIO, to the patient's underlying risk factors for hearing loss, a combination of these factors, or to other factors (see **PRECAUTIONS, Information for Patients**).

“Other events:

The following list includes other adverse events that have been identified during post-marketing use of REVATIO. The list does not include adverse events that are reported from clinical trials and that are listed elsewhere in this section. These events have been chosen for inclusion either due to their seriousness, reporting frequency, lack of clear alternative causation, or a combination of these factors. Because these reactions were reported voluntarily from a population of uncertain size, it is not possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

“Nervous: seizure, seizure recurrence”

5) To change “**What are the possible side effects of REVATIO (sildenafil citrate)**” section of the patient package insert (differences are underlined)

From

The following side effects were reported rarely in men taking sildenafil for the treatment of erectile dysfunction (impotence):

- **decreased eyesight or loss of sight in one or both eyes (NAION).** If you notice a sudden decrease or loss of eyesight, talk to your doctor right away. It is not possible to determine if these events are related to oral medicines for the treatment of erectile dysfunction, including sildenafil, or to other medical problems, or combination of these factors.
- **heart attack, stroke, irregular heartbeats, and death.** Most of these happened in men who already had heart problems.
- **erections that last several hours.** Tell your doctor right away if you have an erection that lasts more than 4 hours.

To

The following side effects were reported rarely in patients taking sildenafil:

- **decreased eyesight or loss of sight in one or both eyes (NAION).** If you notice a sudden decrease or loss of eyesight, talk to your doctor right away. It is not possible to determine if these events are related to oral medicines for the treatment of erectile dysfunction, including sildenafil, or to other medical problems, or combination of these factors.
- **sudden decrease or loss of hearing.** If you notice a sudden decrease or loss of hearing, talk to your doctor right away. It is not possible to determine whether these events are related directly to this class of oral medicines, including sildenafil, or to other diseases or medications, to other factors, or to a combination of factors.
- **heart attack, stroke, irregular heartbeats, and death.** Most of these happened in men who already had heart problems.
- **erections that last several hours.** Tell your doctor right away if you have an erection that lasts more than 4 hours.

Also, to change the following sentence (differences are underlined)

From

The following side effects were reported in patients taking REVATIO. Some these were serious.

To

The following side effects were reported in patients taking REVATIO. Some of these were serious.

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

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

Marketing the product with labeling that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

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 Dan Brum, Pharm.D., MBA, Regulatory Health Project Manager, at (301)796-0578.

Sincerely,

{See appended electronic signature page}

Norman Stockbridge, M.D., Ph.D.
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
this page is the manifestation of the electronic signature.**

/s/

Norman Stockbridge
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