



NDA 21-845/S-003

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

Dear Mr. Clark:

Please refer to your supplemental new drug application dated February 9, 2006 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. In the **PRECAUTIONS/Drug Interactions/Effects of REVATIO on Other Drugs/In vivo studies** section, the fifth paragraph was changed from:

Sildenafil at steady state (80 mg t.i.d.) resulted in a 50% increase in AUC and a 42% increase in  $C_{max}$  of bosentan (125 mg b.i.d.).

To:

In healthy subjects, co-administration of 125 mg b.i.d. bosentan and 80 mg t.i.d. sildenafil resulted in a 63% decrease in AUC of sildenafil and 50% increase in AUC of bosentan.

2. The second bullet of the **PRECAUTIONS/General** section was changed from:

REVATIO should be used with caution in patients with anatomical deformation of the penis (such as angulation, cavernosal fibrosis or Peyronie's disease) or in patients who have conditions, which may predispose them to priapism (such as sickle cell anemia, multiple myeloma or leukemia).

To:

REVATIO should be used with caution in patients with anatomical deformation of the penis (such as angulation, cavernosal fibrosis or Peyronie's disease) or in patients who have conditions, which may predispose them to priapism (such as sickle cell anemia, multiple myeloma or leukemia). In the event of an erection that persists longer than 4 hours, the patient should seek immediate medical assistance. If priapism (painful erections greater than 6 hours in duration) is not treated immediately, penile tissue damage and permanent loss of potency could result.

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.

The final printed labeling (FPL) must be identical to the submitted labeling (package insert included in your submission of February 9, 2006).

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

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/s/

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Norman Stockbridge  
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