021845_Original Appraisal_Package.PDF

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Approval Package for:

APPLICATION NUMBER:

21-845

Trade Name:	Revatio
Generic Name:	Sildenafil citrate
Sponsor:	Pfizer Inc.
Approval Date:	June 3, 2005
Indications:	Provides for the use of Revatio (sildenafil citrate) Tablets for the treatment of pulmonary arterial hypertension (WHO Group I) to improve exercise ability.

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APPLICATION NUMBER:

21-845

APPROVAL LETTER(S)

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-845

Pfizer, Inc.
Attention: Ms. Martha C. Brumfield
235 E. 42nd Street
New York, NY 10017

Dear Ms. Brumfield:

Please refer to your new drug application (NDA) dated December 2, 2004, received December 3, 2004, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Revatio (sildenafil citrate) 20 mg Tablets.

We acknowledge receipt of your submissions dated December 28, 2004 and February 16, April 8 and 27, 2005.

This new drug application provides for the use of Revatio (sildenafil citrate) Tablets for the treatment of pulmonary arterial hypertension (WHO Group I) to improve exercise ability. The enclosed labeling acknowledges that the efficacy of Revatio has not been evaluated in patients currently on bosentan therapy.

We completed our review of this application, as amended. It 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 enclosed labeling (package insert) and the submitted labeling (immediate container and carton labels included in your submission dated December 2, 2004). Marketing the product with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

Please submit an electronic version of the FPL according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDA*. Alternatively, you may submit 20 paper copies of the FPL as soon as it is available but no more than 30 days after it is printed. Individually mount 15 of the copies on heavy-weight paper or similar material. For administrative purposes, designate this submission "**FPL for approved NDA 21-845.**" Approval of this submission by FDA is not required before the labeling is used.

All applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred. We are deferring submission of your pediatric studies for ages 0 to 16 years until June 19, 2007.

We remind you of your postmarketing study commitments in your submission dated June 2, 2005. These commitments are listed below.

1. Because the effects of Revatio on exercise were very similar at all doses you studied, you have committed to study the therapeutic effect of Revatio when administered below the proposed recommended dose of 20 mg t.i.d.

2. Because you excluded from studies patients who were receiving concomitant bosentan or who had failed on bosentan, you have committed to study the safety and efficacy of Revatio when used clinically in combination with bosentan.

We also remind you of your commitment to educate healthcare providers regarding the fact that Revatio contains the same active ingredient (sildenafil citrate) as Viagra, and to highlight the potential for interaction with nitrates. A summary of this plan should accompany your introductory promotional materials.

Submit clinical protocols to your IND for this product. Submit nonclinical and chemistry, manufacturing, and controls protocols and all study final reports to this NDA. In addition, under 21 CFR 314.81(b)(2)(vii) and 314.81(b)(2)(viii), you should include a status summary of each commitment in your annual report to this NDA. The status summary should include expected summary completion and final report submission dates, any changes in plans since the last annual report, and, for clinical studies, number of patients entered into each study. All submissions, including supplements, relating to these postmarketing study commitments must be prominently labeled "**Postmarketing Study Commitment Protocol**", "**Postmarketing Study Commitment Final Report**", or "**Postmarketing Study Commitment Correspondence**."

In addition, submit three copies of the introductory promotional materials that you propose to use for this product. Submit all proposed materials in draft or mock-up form, not final print. Send one copy to this division and two copies of both the promotional materials and the package insert directly to:

Division of Drug Marketing, Advertising,
and Communications, HFD-42
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857

We have not completed validation of the regulatory methods. However, we expect your continued cooperation to resolve any problems that may be identified.

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 contact:

Mr. Russell Fortney
Regulatory Health Project Manager
(301) 594-5311

Sincerely,

{See appended electronic signature page}

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

Enclosure