



NDA 021845/S-016
NDA 022473/S-010
NDA 203109/S-009

SUPPLEMENT APPROVAL

Pfizer, Inc.
Attention: Elina Srulevitch-Chin
Executive Director, Portfolio Lead
Worldwide Safety & Regulatory, GEP NA
445 Easter Point Road
Groton, CT 06340

Dear Ms. Srulevitch-Chin:

Please refer to your Supplemental New Drug Applications (sNDAs) dated and received March 23, 2015, submitted under section 505(b)(1) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Revatio (sildenafil) 20 mg tablets for oral administration (NDA 021845), 10 mg/12.5 mL single use vials for Injection (022473), and 10mg/mL (reconstituted) Oral Suspension (NDA 203109).

We also refer to your amendment dated April 20, 2015.

This supplemental new drug application provides for labeling revised as follows (additions are marked as underlined text and deletions are marked as ~~strike through text~~):

In the Package Insert:

1. In **HIGHLIGHTS**, the following text was added/deleted:

-----RECENT MAJOR CHANGES-----	
INDICATIONS AND USAGE (1)	01/2014
DOSAGE AND ADMINISTRATION, REVATIO Tablets and Oral Suspension (2.1)	01/2014
DOSAGE AND ADMINISTRATION, REVATIO Injection (2.2)	01/2014
DOSAGE AND ADMINISTRATION, Reconstitution of the Powder for Oral Suspension (2.3)	01/2014
WARNINGS AND PRECAUTIONS, Visual Loss (5.5)	03/2014
CONTRAINDICATIONS (4)	04/2015

2. In **HIGHLIGHTS/CONTRAINDICATIONS**, the first bullet was updated to read:
 - Use with organic nitrates or riociguat (4)
3. Under **CONTRAINDICATIONS**, the following bullet was added:
 - Concomitant use of riociguat, a guanylate cyclase stimulator. PDE5 inhibitors, including sildenafil, may potentiate the hypotensive effects of riociguat.
4. The revision date and version number were updated.

In the PPI:

1. Under **What is the most important information I should know about REVATIO?**, the following text was added:

Never take REVATIO with any nitrate ~~medicines~~ or guanylate cyclase stimulator medicines. Your blood pressure could drop quickly to an unsafe level.

Nitrate medicines include:

- **Medicines that treat chest pain (angina)**
- **Nitroglycerin in any form including tablets, patches, sprays, and ointments**
- **Isosorbide mononitrate or dinitrate**
- **Street drugs called “poppers” (amyl nitrate or nitrite)**

Guanylate cyclase stimulators include:

- **Riociguat (Adempas)**

Ask your doctor or pharmacist if you are not sure if you are taking a nitrate ~~medicine~~ or a guanylate cyclase stimulator medicine.

2. Under who should not take REVATIO?, the following bullet was added:
 - **take guanylate cyclase stimulator medicines. See “What is the most important information I should know about REVATIO?”**
3. Under Especially tell your doctor if you take, the following bullet was added:
 - **Riociguat (Adempas). See “What is the most important information I should know about REVATIO?”**
4. The revision date and version number were updated.

There are no other changes from the last approved package insert.

We have completed our review of these supplemental applications, as amended, and they are approved, effective on the date of this letter, for use as recommended in the enclosed, agreed-upon labeling text.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, submit the content of labeling [21 CFR 314.50(1)] in structured product labeling (SPL) format using the FDA automated drug registration and listing system (eLIST), as described at <http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>. Content of labeling must be identical to the enclosed labeling (text for the package insert), with the addition of any labeling changes in pending “Changes Being Effected” (CBE) supplements, as well as annual reportable changes not included in the enclosed labeling.

Information on submitting SPL files using eLIST may be found in the guidance for industry titled “SPL Standard for Content of Labeling Technical Qs and As” at <http://www.fda.gov/downloads/DrugsGuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf>.

The SPL will be accessible from publicly available labeling repositories.

Also within 14 days, amend all pending supplemental applications for this NDA, including CBE supplements for which FDA has not yet issued an action letter, with the content of labeling [21 CFR 314.50(l)(1)(i)] in MS Word format, that includes the changes approved in this supplemental application, as well as annual reportable changes and annotate each change. To facilitate review of your submission, provide a highlighted or marked-up copy that shows all changes, as well as a clean Microsoft Word version. The marked-up copy should provide appropriate annotations, including supplement number(s) and annual report date(s).

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit the following, in triplicate, (1) a cover letter requesting advisory comments, (2) the proposed materials in draft or mock-up form with annotated references, and (3) the package insert(s) to:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Drug Marketing, Advertising, and Communications
5901-B Ammendale Road
Beltsville, MD 20705-1266

You must submit final promotional materials and package insert(s), accompanied by a Form FDA 2253, at the time of initial dissemination or publication [21 CFR 314.81(b)(3)(i)]. Form FDA 2253 is available at <http://www.fda.gov/opacom/morechoices/fdaforms/cder.html>; instructions are provided on page 2 of the form. For more information about submission of promotional materials to the Division of Drug Marketing, Advertising, and Communications (DDMAC), see <http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm>.

All promotional materials that include representations about your drug product must be promptly revised to be consistent with the labeling changes approved in this supplement, including any new safety information [21 CFR 314.70(a)(4)]. The revisions in your promotional materials should include prominent disclosure of the important new safety information that appears in the revised package labeling. Within 7 days of receipt of this letter, submit your statement of intent to comply with 21 CFR 314.70(a)(4) to the address above or by fax to 301-847-8444.

REPORTING REQUIREMENTS

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:

Lori Anne Wachter, RN, BSN
Regulatory Project Manager for Safety
(301) 796-3975

NDA 021845/S-016
NDA 022473/S-010
NDA 203109/S-009
Page 4

Sincerely,

{See appended electronic signature page}

Mary Ross Southworth, PharmD.
Deputy Director for Safety
Division of Cardiovascular and Renal Products
Office of Drug Evaluation 1
Center for Drug Evaluation and Research

ENCLOSURE:
Content of Labeling

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

MARY R SOUTHWORTH
04/27/2015