DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 21134/S-005

SUPPLEMENT APPROVAL

Pfizer, Inc.
Attention: Tricia Douglas
Manager, Worldwide Regulatory Strategy
235 East 42nd Street
New York, NY 10017

Dear Ms. Douglas:

Please refer to your Supplemental New Drug Application (sNDA) dated June 14, 2011, received June 14, 2011, submitted under section 505(b)/(1) of the Federal Food, Drug, and Cosmetic Act for Nitrostat (nitroglycerin, USP) Sublingual Tablets, 0.3, 0.4, and 0.6 mg.

This "Prior Approval" supplemental new drug application provides for addition of all PDE 5 inhibitors in the label as well as a new patient package insert (PPI). Labeling has been revised as follows:

1. Under **CONTRAINDICATIONS**, the third paragraph was changed from:

   Administration of Nitrostat is contraindicated in patients who are using a phosphodiesterase-5 (PDE-5) inhibitor (*e.g.*, sildenafil citrate) since these compounds have been shown to potentiate the hypotensive effects of organic nitrates.

   To read as follows:

   Administration of NITROSTAT is contraindicated in patients who are using a phosphodiesterase-5 (PDE-5) inhibitor (e.g., sildenafil citrate, tadalafil, vardenafil hydrochloride) since these compounds have been shown to potentiate the hypotensive effects of organic nitrates.

2. Under **PRECAUTIONS, Drug Interactions**, the eighth paragraph was changed from:

   Administration of nitroglycerin is contraindicated in patients who are using Viagra (sildenafil citrate). Viagra has been shown to potentiate the hypotensive effects of organic nitrates.

   To read as follows:

   Administration of nitroglycerin is contraindicated in patients who are using PDE-5 inhibitors (e.g., sildenafil citrate, tadalafil, vardenafil hydrochloride). These compounds have been shown to potentiate the hypotensive effects of organic nitrates.

3. The PPI has been updated with information with all PDE-% inhibitors (e.g. tadalafil and vardenafil hydrochloride).

4. Minor editorial changes have been made throughout the label.

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

We remind you of the requested changes to your container labels and carton described in our November 12, 2009 letter and approved on July 12, 2010. According to your email of July 19, 2011, the new carton and container labeling had not been implemented. These changes were requested based on medication error reports involving unintentional overdoses by patients and healthcare providers and improper storage and use of the drug. We continue to receive reports of these errors and request that you implement these changes as soon as possible. Please update us on your implementation plan.

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(l)] 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, 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 Alexis Childers, Regulatory Project Manager, at (301) 796-0442.

Sincerely,

{See appended electronic signature page}

Mary Ross Southworth, Pharm.D.
Deputy Director for Safety
Office of Drug Evaluation I
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
07/21/2011