DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 018154/S-026

SUPPLEMENT APPROVAL

Pfizer Inc.
Attention: Marcio de Godoy, MBA, PharmD, PhD
Senior Manager, Worldwide Safety and Regulatory
500 Arcola Road
G-4347
Collegeville, PA 19426

Dear Dr. De Godoy:

Please refer to your Supplemental New Drug Application (sNDA) dated and received October 10, 2014, submitted under section 505(b)(1) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Loniten (minoxidil) 2.5 mg and 10 mg Tablets.

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

1. Under **CLINICAL PHARMACOLOGY**, the following text was added:

Absorption and Metabolism
Minoxidil is at least 90% absorbed from the GI tract in experimental animals and man. Plasma levels of the parent drug reach maximum within the first hour and decline rapidly thereafter. The average plasma half-life in man is 4.2 hours. Approximately 90% of the administered drug is metabolized, predominantly by conjugation with glucuronic acid at the N-oxide position in the pyrimidine ring, but also by conversion to more polar products. Known metabolites exert much less pharmacologic effect than minoxidil itself; all are excreted principally in the urine. Minoxidil does not bind to plasma proteins and does not cross the blood brain barrier. ~~, and it~~ its renal clearance corresponds to the glomerular filtration rate. In the absence of functional renal tissue, minoxidil and its metabolites can be removed by hemodialysis.

2. Under **PRECAUTIONS**, the following information was added:

Pregnancy
Teratogenic Effects
Pregnancy Category C. Oral administration of minoxidil has been associated with evidence of increased fetal resorption in rabbits, but not rats, when administered at five times the maximum recommended oral antihypertensive human dose. There was no evidence of teratogenic effects in rats and rabbits. Subcutaneous administration of minoxidil to pregnant rats at 80 mg/kg/day was maternally toxic but not teratogenic. Higher subcutaneous doses produced evidence of developmental toxicity. There are no adequate and well controlled studies in pregnant women. LONITEN should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Neonatal hypertrichosis has been reported following exposure to minoxidil during pregnancy.

3. Under **ADVERSE REACTIONS**, the following text was added:

   Allergic—Rashes have been reported, including rare reports of bullous eruptions, toxic epidermal necrolysis, and Stevens-Johnson Syndrome.

4. The revision date and version number was updated.

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

We have completed our review of this supplemental application, as amended, and it is 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(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 (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

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
01/13/2015