



NDA 20-634/S-050
NDA 20-635/S-054
NDA 21-721/S-018

Ortho-McNeil Pharmaceutical, Inc.
c/o Johnson & Johnson Pharmaceutical Research & Development, L.L.C.
ATTN: Ms. Alysia Baldwin-Ferro
Senior Director, Regulatory Affairs
920 U.S. Highway 202, P.O. Box 300
Raritan, NJ 08869-0602

Dear Ms. Baldwin-Ferro:

Please refer to your supplemental new drug applications dated and received on November 8, 2007 and submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for the following:

NDA Number	Supplement Number	Drug Product
20-634	050	Levaquin [®] (levofloxacin) Tablets, 250 mg, 500 mg, and 750 mg
20-635	054	Levaquin [®] (levofloxacin) Injection and Levaquin [®] (levofloxacin in 5% dextrose) Injection, 5 mg/mL
21-721	018	Levaquin [®] (levofloxacin) Oral Solution, 25 mg/mL

We acknowledge receipt of your submissions dated November 27, 2007.

These “Special Supplements - Changes Being Effected” supplemental applications propose revising the content of labeling for the package insert to ensure consistency in the communication of the risk of phototoxicity associated with the use of fluoroquinolones, including levofloxacin.

We have completed our review of these applications, as amended. These applications are approved, effective on the date of this letter, for use as recommended in the agreed-upon labeling text with a minor editorial revision listed below:

- The **5. WARNINGS AND PRECAUTIONS/5.10 Photosensitivity/Phototoxicity** section was modified as follows (additions are noted with underline and deletions noted with ~~strikethrough~~):

Moderate to severe photosensitivity/phototoxicity reactions, the latter of which may manifest as exaggerated sunburn reactions (e.g., burning, erythema, exudation, vesicles, blistering, edema) involving areas exposed to light (typically the face, “V” area of the neck, extensor surfaces of

the forearms, dorsa of the hands), can be associated with the use of quinolones after sun or UV light exposure. Therefore, excessive exposure to these sources of light should be avoided. Drug therapy should be discontinued if photosensitivity/phototoxicity occurs (See **ADVERSE REACTIONS/Post-Marketing Adverse Events**).

The revisions to the package insert were as follows (additions are noted with underline and deletions noted with ~~strikethrough~~):

1. The **5. WARNINGS AND PRECAUTIONS/5.10 Photosensitivity/Phototoxicity** section was modified as follows:

~~Moderate to severe phototoxicity reactions have been observed in patients exposed to direct sunlight while receiving drugs in this class. Excessive exposure to sunlight should be avoided. However, in clinical trials with LEVAQUIN®, phototoxicity has been observed in less than 0.1% of patients. Therapy should be discontinued if phototoxicity (e.g., a skin eruption) occurs [see Adverse Reactions (6.3); Patient Counseling Information (17.3)].~~ Moderate to severe photosensitivity/phototoxicity reactions, the latter of which may manifest as exaggerated sunburn reactions (e.g., burning, erythema, exudation, vesicles, blistering, edema) involving areas exposed to light (typically the face, “V” area of the neck, extensor surfaces of the forearms, dorsa of the hands), can be associated with the use of quinolones after sun or UV light exposure. Therefore, excessive exposure to these sources of light should be avoided. Drug therapy should be discontinued if photosensitivity/phototoxicity occurs (See **ADVERSE REACTIONS/Post-Marketing Adverse Events**).

2. The **6. ADVERSE REACTIONS/6.1 Serious and Otherwise Important Adverse Reactions** section was modified as follows:

The following serious and otherwise important adverse drug reactions are discussed in greater detail in other sections of labeling:

- Photosensitivity/Phototoxicity [see *Warnings and Precautions*(5.10)]

3. In the **6. ADVERSE REACTIONS/6.3 Post-Marketing Adverse Events** section, the following was modified:

System/Organ Class	Adverse Reaction
Skin and Subcutaneous Tissue Disorders	bullous eruptions to include: Stevens-Johnson Syndrome toxic epidermal necrolysis erythema multiforme <i>[see Warnings and Precautions (5.2)]</i> photosensitivity/ <u>phototoxicity reaction</u> [see <i>Warnings and Precautions (5.10)</i>] leukocytoclastic vasculitis

4. The **17. PATIENT COUNSELING INFORMATION/17.3 Serious and Potentially Serious Adverse Reactions** section was modified as follows:

Patients should be informed of the following serious adverse reactions that have been associated with LEVAQUIN® or other quinolone use:

- Phototoxicity: Patients should be advised ~~to avoid excessive sunlight or artificial ultraviolet light while receiving LEVAQUIN® and to discontinue therapy if phototoxicity (i.e., skin eruption) occurs.~~ that photosensitivity/phototoxicity has been reported in patients receiving quinolone antibiotics. Patients should minimize or avoid exposure to natural or artificial sunlight (tanning beds or UVA/B treatment) while taking quinolones. If patients need to be outdoors when taking quinolones, they should wear loose-fitting clothes that protect skin from sun exposure and discuss other sun protection measures with their physician. If a sunburn like reaction or skin eruption occurs, patients should contact their physician.

5. The **17. PATIENT COUNSELING INFORMATION/17.5 FDA-Approved Patient Labeling/Patient Information About Levaquin/What are possible side effects of Levaquin?** section was modified as follows:

~~Some quinolone antibiotics have been associated with the development of phototoxicity (“sunburns” and “blistering sunburns”) following exposure to sunlight or other sources of ultraviolet light such as artificial ultraviolet light used in tanning salons. LEVAQUIN® has been infrequently associated with phototoxicity. You should avoid excessive exposure to sunlight or artificial ultraviolet light while you are taking LEVAQUIN®. Sun sensitivity (photosensitivity), which can appear as skin eruption or severe sunburn, can occur in some patients taking quinolone antibiotics after exposure to sunlight or artificial ultraviolet (UV) light (e.g., tanning beds). LEVAQUIN® has been infrequently associated with photosensitivity. Avoid excessive exposure to sunlight or artificial UV light while taking LEVAQUIN®. Use a sunscreen and wear protective clothing if out in the sun. If photosensitivity develops, contact your physician.~~

6. Minor editorial changes throughout the labeling.

CONTENT OF LABELING

As soon as possible, please submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format as described at <http://www.fda.gov/oc/datacouncil/spl.html> that is identical to the enclosed labeling (text for the package insert and text for the patient package insert). Upon receipt, we will transmit this version to the National Library of Medicine for public dissemination. For administrative purposes, please designate these submissions, “**SPL for approved NDA 20-634/S-050, NDA 20-635/S-054, and NDA 21-721/S-018.**”

LETTERS TO HEALTH CARE PROFESSIONALS

If you issue a letter communicating important information about these drug products (i.e., a “Dear Health Care Professional” letter), we request that you submit a copy of the letter to these NDAs and a copy to the following address:

MEDWATCH
Food and Drug Administration
5515 Security Lane
HFD-001, Suite 5100
Rockville, MD 20852

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, call Rebecca D. Saville, Pharm.D., Regulatory Project Manager, at (301) 796-1600.

Sincerely,

{See appended electronic signature page}

Renata Albrecht, M.D.
Director
Division of Special Pathogen and Transplant Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research

Enclosure

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

/s/

Renata Albrecht
12/13/2007 03:54:11 PM