DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-085/S-038
NDA 21-277/S-031

Bayer Pharmaceuticals Corporation
Attention: Janet Herrington, Ph.D.
Deputy Director, Regulatory Affairs
400 Morgan Lane
West Haven, CT 06516

Dear Dr. Herrington:

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

NDA #	Drug Product	Supplement Number	Date of supplement	Date of receipt
21-085	Avelox® (moxifloxacin hydrochloride) Tablets	S-038	November 19, 2007	November 20, 2007
21-277	Avelox® (moxifloxacin hydrochloride in NaCl injection) I.V.	S-031	November 19, 2007	November 21, 2007

These "Special Supplement - Changes Being Effected" supplemental new drug applications provide for revisions to the package insert for Avelox® to ensure consistency in the communication of the risks of photosensitivity/phototoxicity with the use of fluoroquinolone products, including moxifloxacin.

The following revisions (~~strikethrough~~ = deleted and underlined = added) to the text for the package insert for Avelox were proposed in these supplemental applications and incorporated in the November 19, 2007 submissions:

1. The following paragraph was added to the **CLINICAL PHARMACOLOGY/ Photosensitivity Potential** subsection:

   Photosensitivity Potential
   It is difficult to ascribe relative photosensitivity/phototoxicity among various fluoroquinolones during actual patient use because other factors play a role in determining a subject's susceptibility to this adverse event such as: a patient's skin pigmentation, frequency and duration of sun and artificial ultraviolet light (UV) exposure, wearing of sunscreen and protective clothing, the use of other concomitant drugs and the dosage and duration of fluoroquinolone therapy (See **ADVERSE REACTIONS** and **ADVERSE REACTIONS/Post-Marketing Adverse Event Reports).**

2. The following text was added to the **PRECAUTIONS/General** subsection:

   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 quinolone antibiotics after sun or UV light exposure. Therefore, excessive exposure to these sources of light should be avoided. Drug therapy should be discontinued if phototoxicity occurs (See **ADVERSE REACTIONS** and **ADVERSE REACTIONS/ Post-Marketing Adverse Event Reports**).

3. The following text was modified in the **PRECAUTIONS/Information for Patients** subsection:

   - that photosensitivity/phototoxicity has been reported in patients receiving quinolones. 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 while using quinolones, they should wear loose-fitting clothes that protect skin from sun exposure and discuss other sun protection measures with their physician. ~~In keeping with good medical practice, avoid excessive sunlight or artificial ultraviolet light (e.g., tanning beds).~~ If a sunburn-like reaction or skin eruption occurs, patients should contact their physician (see **CLINICAL PHARMACOLOGY/ Photosensitivity Potential**)

4. The **ADVERSE REACTIONS** section was modified as follows:

   Additional clinically relevant rare events, judged by investigators to be at least possibly drug-related, that occurred in less than 0.1% of moxifloxacin treated patients were: abnormal dreams…., pelvic pain, peripheral edema, photosensitivity/phototoxicity reactions, pseudomembranous colitis,…

5. In the **ADVERSE REACTIONS/Post-Marketing Adverse Event Reports** subsection, the following was modified:

   Photosensitivity/phototoxicity reaction (see **PRECAUTIONS)**

6. The **"Patient Package Insert"/** "**What are possible side effects of AVELOX?"** was modified as follows:

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

We completed our review of these applications, as amended. This application is approved, effective on the date of this letter, for use as recommended in the agreed-upon labeling text and with the minor editorial revision agreed upon during the February 6, 2008, communications between Kristen Miller, Pharm.D. and yourself listed below:

1. The third to last bullet in the **PRECAUTIONS/Information for Patients** subsection was modified as follows:

   - that photosensitivity/phototoxicity has been reported in patients receiving quinolones [redacted] 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 while using 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 (see **CLINICAL PHARMACOLOGY/ Photosensitivity Potential**)

Within 21 days of the date of this letter, submit 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 in content to the enclosed labeling text. Upon receipt, we will transmit that version to the National Library of Medicine for public dissemination. For administrative purposes, please designate these submissions "**SPL for approved supplement NDA 21-085/S-038 and NDA 21-277/S-031**."

If you issue a letter communicating important information about this drug product (i.e., a "Dear Health Care Professional" letter), we request that you submit a copy of the letter to this NDA and a copy to the following address:

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

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 Kristen Miller, 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

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