DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-473/S-023

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 application dated November 19, 2007, received on November 20, 2007, and submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for the following:

NDA Number	Supplement Number	Drug Product
21-473	023	CIPRO® XR (ciprofloxacin extended-release) Tablets, 500 mg and 1000 mg

This "Special Supplement - Changes Being Effected" supplemental application proposes 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 ciprofloxacin extended-release.

We have completed our review of this application. This application is approved, effective on the date of this letter, for use as recommended in the agreed-upon labeling text with minor editorial revisions listed below (additions are noted with underline and deletions noted with ~~strikethrough~~):

1. The second paragraph of the **PRECAUTIONS** section was modified as follows:

   Photosensitivity/Phototoxicity: 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 fifth bullet of 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.

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

1. The second paragraph of the **PRECAUTIONS** section was modified as follows:

   ~~Moderate to severe phototoxicity manifested as an exaggerated sunburn reaction has been observed in patients who are exposed to direct sunlight while receiving some members of the quinolone class of drugs. Excessive sunlight should be avoided. Therapy should be discontinued if phototoxicity occurs.~~ **Photosensitivity/Phototoxicity:** 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 fifth bullet of the **PRECAUTIONS/Information for Patients** subsection was modified as follows:

   - ~~to avoid excessive sunlight or artificial ultraviolet (UV) light while receiving Cipro XR and to discontinue therapy if phototoxicity occurs.~~ 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. If a sunburn-like reaction or skin eruption occurs, patients should contact their physician.

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

   Additional uncommon events, judged by investigators to be at least possibly drug-related, that occurred in less than 1% of CIPRO XR treated patients were:

   SKIN/~~APPENDAGES~~HYPERSENSIVITY: dry skin, maculopapular rash, photosensitivity/phototoxicity reactions, pruritus, rash, skin disorder, urticaria, vesiculobullous rash

4. In the sixth paragraph of the **ADVERSE REACTIONS** section that lists postmarketing adverse reactions, photosensitivity/phototoxicity reaction was added alphabetically to the list.

5. In the **"Patient Information About Cipro XR"/** "**What are possible side effects of Cipro XR?"** subsection, the following paragraph was modified as follows:

   ~~Some patient taking quinolone antibiotics may become more sensitive to sunlight or ultraviolet light such as that used in tanning salons. You should avoid excessive exposure to sunlight or ultraviolet light while you are taking CIPRO.~~ 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). CIPRO XR has been infrequently associated with photosensitivity. Avoid excessive exposure to sunlight or artificial UV light while taking CIPRO XR. Use a sunscreen and wear protective clothing if out in the sun. If photosensitivity develops, contact your physician.

6. Minor editorial corrections 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 this submission, "**SPL for approved NDA 21-473/S-023**."

LETTERS TO HEALTH CARE PROFESSIONALS

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 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

1/18/2008 05:59:11 AM