



NDA 19-537/S-067
NDA 20-780/S-025

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 Number	Supplement Number	Drug Product	Submission Date	Receipt Date
19-537	S-067	CIPRO [®] (ciprofloxacin hydrochloride) Tablets, 250 mg, 500 mg, 750 mg	November 19, 2007	November 20, 2007
20-780	S-025	CIPRO [®] (ciprofloxacin hydrochloride) Oral Suspension, 5% and 10%	November 19, 2007	November 21, 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 ciprofloxacin.

We have completed our review of these applications. These applications are 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 ~~strike through~~):

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

- 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.

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

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

~~**Phototoxicity:** 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 fourth bullet of the **PRECAUTIONS/Information for Patients** subsection was modified as follows:

- ~~to avoid excessive sunlight or artificial ultraviolet (UV) light while receiving ciprofloxacin 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 medically important events that occurred in less than 1% of ciprofloxacin patients are listed below:

- **SKIN/HYPERSENSITIVITY:** allergic reaction, pruritus, urticaria, photosensitivity/phototoxicity reaction, flushing, fever, chills, angioedema, edema of the face, neck, lips, conjunctivae or hands, cutaneous candidiasis, hyperpigmentation, erythema nodosum, sweating

4. In the **ADVERSE REACTIONS/Postmarketing Adverse Events** subsection, photosensitivity/phototoxicity reaction was added alphabetically to the list of adverse events.
5. In the **“Patient Information About Cipro”/ “What are possible side effects of Cipro?”** 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 has been infrequently associated with photosensitivity. Avoid excessive exposure to sunlight or artificial UV light while taking CIPRO. Use a sunscreen and wear protective clothing if out in the sun. If photosensitivity develops, contact your physician.

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 19-537/S-067 and NDA 20-780/S-025.”**

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
1/18/2008 05:58:19 AM