DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-744/S-005

Depomed, Inc.
Attention: Mr. Jeff Miller
Vice President,
Regulatory Affairs and Quality Assurance
1360 O'Brien Drive
Menlo Park, CA 94025-1436

Dear Mr. Miller:

Please refer to your supplemental new drug application submitted on May 14, 2007, received on May 15, 2007, under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Proquin XR® (ciprofloxacin hydrochloride) Extended-Release Tablets, 500 mg.

This "Changes Being Effected" supplemental new drug application provides for revisions to the package insert for Proquin XR® to provide updated information regarding the risks of phototoxicity. This supplement was submitted in response to the Supplement Request letter issued by the Division on March 2, 2007.

The supplemental application provides for revisions as follows (deletions are ~~strikethrough~~ and additions are underlined):

1. The **PRECAUTIONS**/**General** subsection was modified as follows:

   ~~**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 quinolone antibiotics after sun or UV light exposure. Therefore, excessive exposure to these sources of light should be avoided. ~~manifested as an exaggerated sunburn reaction has been observed in patients who are exposed to direct sunlight while being treated with some members of the quinolone class of drugs. Excessive sunlight should be avoided.~~ Drug t~~T~~herapy ~~with ciprofloxacin~~ should be discontinued if phototoxicity occurs. (See **ADVERSE REACTIONS and ADVERSE REACTIONS/Post-Marketing Adverse Events)**

2. The **PRECAUTIONS**/**Information for Patients** subsection was modified as follows:

   - ~~to avoid excessive sunlight or artificial ultraviolet (UV) light while receiving Proquin XR and to discontinue therapy if phototoxicity 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 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. In the **ADVERSE REACTIONS s**ection, the following was modified:

   Additional uncommon events, judged by the investigator to be at least possibly drug- related, occurring at any time during the study in less than 1% of Proquin XR-treated patients were:

   Skin/Subcutaneous Tissue Disorders: rash, photosensitivity/phototoxicity reaction, pruritus, urticaria.

4. In the **ADVERSE REACTIONS/ Reported Post-Marketing Adverse Events with Other Formulations of Ciprofloxacin** subsection, the following was added to the alphabetical list of adverse events:

   …phlebitis, phobia, photosensitivity/phototoxicity reaction (see **PRECAUTIONS),** pleural effusion,…

5. In the **"Patient Package Insert"/** "**What are possible side effects of Proquin XR?"** the following two sentences were replaced with the following paragraph:

   ~~Some patients 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 Proquin XR.~~

   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). Proquin XR has been infrequently associated with photosensitivity. Avoid excessive exposure to sunlight or artificial UV light while taking Proquin XR. Use a sunscreen and wear protective clothing if out in the sun. If photosensitivity develops, contact your physician.

We completed our review of this application, 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 minor editorial revisions agreed upon during the August 24, 2007, correspondence between Kristen Miller, Pharm.D. and Sean Delaney, RAC listed below:

1. The **HOW SUPPLIED** section was modified as follows:

   Store Proquin XR at 25 °C (77 °F); excursion permitted to 15-30 °C (59-86 °F) [see USP Controlled Room Temperature]

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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