DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 19-735/S-052, S-053

Johnson & Johnson Pharmaceutical Research & Development, L.L.C.
Attention: Robyn S. Thomas
Regulatory Affairs
920 Route 202 South
P.O. Box 300
Raritan, NJ 08869-0602

Dear Ms. Thomas:

Please refer to your supplemental new drug applications dated March 19, 2004, received March 23, 2004, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for FLOXIN® (ofloxacin tablets) Tablets, 200 mg, 300 mg, 400 mg.

We acknowledge receipt of your submissions dated April 9, 2004 and August 23, 2004.

These "Changes Being Effected" (CBE) supplemental new drug applications provide for the addition of quinolone class labeling in **WARNINGS** and **PRECAUTIONS**, **Information for Patients** as was requested in the supplement request letter dated November 26, 2003 and the facsimiles from the Division dated March 10, 2004 and July 12, 2004.

These CBE supplemental new drug applications provide for the following revisions to the package insert:

1. "FLOXIN® (ofloxacin) Tablets" was changed to "FLOXIN® (ofloxacin tablets) Tablets" throughout the label.

2. References to "Videx® (Didanosine) chewable/ buffered tablets or the pediatric powder for oral solution" have been changed to just "Videx® (didanosine)" throughout the label.

3. **WARNINGS**

- A **Peripheral neuropathy** subsection was added to read:

> **Peripheral neuropathy:** Rare cases of sensory or sensorimotor axonal polyneuropathy affecting small and/or large axons resulting in paresthesias, hypoesthesias, dysesthesias and weakness have been reported in patients receiving quinolones, including ofloxacin. Ofloxacin should be discontinued if the patient experiences symptoms of neuropathy including pain, burning, tingling, numbness, and/or weakness or other alterations of sensation including light touch, pain, temperature, position sense, and vibratory sensation in order to prevent the development of an irreversible condition.

- The **Tendon effects** subsection was revised to read:

> **Tendon effects:** Ruptures of the shoulder, hand, ~~and~~ Achilles tendon or other tendons that required surgical repair or resulted in prolonged disability have been reported in patients receiving quinolones, including ofloxacin. Post-marketing surveillance reports indicate that the risk may be increased in patients receiving corticosteroids, ~~with ofloxacin and other quinolones~~ especially the elderly. (see ***PRECAUTIONS***). Ofloxacin should be discontinued if the patient experiences pain, inflammation, or rupture of a tendon. Patients should rest and refrain from exercise until the diagnosis of tend~~i~~onitis or tendon rupture has been confidently excluded. Tendon rupture can occur ~~at any time~~ during or after therapy with quinolones, including ofloxacin.

4. PRECAUTIONS

- A **Torsades de pointes** subsection was added to read:

> **Torsades de pointes:** Some quinolones, including ofloxacin, have been associated with prolongation of the QT interval on the electrocardiogram and infrequent cases of arrhythmia. Rare cases of torsades de pointes have been spontaneously reported during post-marketing surveillance in patients receiving quinolones, including ofloxacin. Ofloxacin should be avoided in patients with known prolongation of the QT interval, patients with uncorrected hypokalemia, and patients receiving class IA (quinidine, procainamide), or class III (amiodarone, sotalol) antiarrhythmic agents.

- The following bullet concerning peripheral neuropathy was added under **Information for Patients:**

  - that peripheral neuropathies have been associated with ofloxacin use. If symptoms of peripheral neuropathy including pain, burning, tingling, numbness, and/or weakness develop, they should discontinue treatment and contact their physicians;

- The following paragraph was added to the **Geriatric Use** subsection:

> Elderly patients may be more sensitive to drug-associated effects on the QT interval. Therefore, precaution should be taken when using ofloxacin with concomitant drugs that can result in prolongation of the QT interval (e.g. class IA or class III antiarrhythmics) or in patients with risk factors for Torsade de pointes (e.g. known QT prolongation, uncorrected hypokalemia). (See ***PRECAUTIONS: GENERAL:*** Torsades de pointes)

5. HOW SUPPLIED

- The first two sentences in this section were revised to read:

> FLOXIN® (ofloxacin tablets) Tablets are supplied as 200 mg light yellow, 300 mg white, and 400 mg pale gold oval, straight-edged, ~~film~~ coated tablets. Each tablet is distinguished by an imprint of "FLOXIN" and the appropriate strength.

We completed our review of these applications, as amended, and they are approved effective on the date of this letter.

The final printed labeling (FPL) must be identical to the enclosed draft labeling (text for the package insert submitted August 23, 2004).

The electronic labeling rule published December 11, 2003 (68 FR 69009) requires submission of labeling content in electronic format effective June 8, 2004. For additional information, consult the following guidances for industry regarding electronic submissions: *Providing Regulatory Submissions in Electronic Format - NDAs (January 1999) and Providing Regulatory Submissions in Electronic Format – Content of Labeling* (February 2004). The guidances specify that labeling is to be submitted in *pdf* format. To assist in our review, we request that labeling also be submitted in MS Word format. If formatted copies of all labeling pieces (i.e., package insert, patient package insert, container labels, and carton labels) are submitted electronically, labeling does not need to be submitted in paper. For administrative purposes, these submissions should be designated **"FPL for approved supplement NDA 19-735/S-052, S-053."** Approval of this submission by FDA is not required before the labeling is used.

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, HFD-410
FDA
5600 Fishers Lane
Rockville, MD 20857

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 Robin Anderson, R.N., M.B.A., Labeling Reviewer at (301) 827-2127.

Sincerely,

{See appended electronic signature page}

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

Enclosure

PROPOSED TEXT OF THE LABELING FOR FLOXIN

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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