DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 020634/S-065
NDA 020635/S-071
NDA 021721/S-032

SUPPLEMENT APPROVAL

Janssen Research & Development, LLC
Attention: Andrea F. Kollath, DVM
Director, Global Regulatory Affairs
1000 Route 202 South
P.O. Box 300
Raritan, NJ 08869

Dear Dr. Kollath:

Please refer to your Supplemental New Drug Applications (sNDA) dated and received July 26, 2013, submitted under section 505(b) the Federal Food, Drug, and Cosmetic Act (FDCA) for the following:

NDA #	Supplement #	Drug Product	Dosage
20-634	065	Levaquin (levofloxacin) Tablets	250 mg, 500 mg, and 750 mg
20-635	071	Levaquin (levofloxacin) Injection	25 mg/mL and 5 mg/mL
21-721	032	Levaquin (levofloxacin) Oral Solution	25 mg/mL

We also refer to our approval letter dated August 14, 2013, which contained the following error: the United States Package Insert (USPI) version August 2013, dosing information from Table 1 on page 7 for "Inhalational Anthrax (Post-Exposure), adult and pediatric patients" was inadvertently deleted. Table 1 is titled "Dosage in Adult Patients with Normal Renal Function (creatinine clearance $\geq$ 50 mL/min)". The correct dosing was still included in the highlights section of the USPI on page 1.

The labeling appended to this replacement approval letter incorporates the correction of the error. The effective approval date will remain August 14, 2013, the date of the original approval letter.

We also refer to our letter dated June 27, 2013, notifying you, under Section 505(o)(4) of the FDCA, of new safety information that we believe should be included in labeling for the systemic fluoroquinolone antibacterial class. This information pertains to the risk of irreversible peripheral neuropathy.

These "Prior Approval" supplemental new drug applications provide for safety labeling changes to the **WARNINGS AND PRECAUTIONS** Section (5), **Peripheral Neuropathy (5.8)**

subsection, **ADVERSE REACTIONS** Section (6)**, Serious and Otherwise Important Adverse Reactions (6.1)** and **Postmarketing Experience (6.3)** subsections, **PATIENT COUNSELING INFORMATION** Section, **Serious and Potentially Serious Adverse Reactions (17.3)** subsection**, MEDICATION GUIDE** (Under "**What are the possible side effects of LEVAQUIN?**"), consistent with our June 27, 2013, letter.

We have completed our review of these supplemental applications. They are approved, effective on the date of this letter, for use as recommended in the enclosed, agreed-upon labeling text and with the revision listed below.

Delete ~~uveitis~~ from the **ADVERSE REACTIONS Section (6), Postmarketing Experience subsection (6.3), Table 8,** Eye Disorders.

We note that your July 26, 2013, submission includes final printed labeling (FPL) for package insert and Medication Guide. We have not reviewed this FPL. You are responsible for assuring that the wording in this printed labeling is identical to that of the approved content of labeling in the structured product labeling (SPL) format.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format using the FDA

automated drug registration and listing system (eLIST), as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm. Content of labeling must be identical to the enclosed labeling (text for the package insert, Medication Guide), with the addition of any labeling changes in pending "Changes Being Effected" (CBE) supplements, as well as annual reportable changes not included in the enclosed labeling. Information on submitting SPL files using eList may be found in the guidance for industry titled "SPL Standard for Content of Labeling Technical Qs and As at http://www.fda.gov/downloads/DrugsGuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf

The SPL will be accessible from publicly available labeling repositories.

Also within 14 days, amend all pending supplemental applications that include labeling changes for these NDAs, including CBE supplements for which FDA has not yet issued an action letter, with the content of labeling [21 CFR 314.50(l)(1)(i)] in MS Word format, that include the changes approved in these supplemental applications, as well as annual reportable changes and annotate each change. To facilitate review of your submission, provide a highlighted or marked-up copy that shows all changes, as well as a clean Microsoft Word version. The marked-up copy should provide appropriate annotations, including supplement number(s) and annual report date(s).

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 Susmita Samanta, Safety Regulatory Project Manager, at (301) 796-0803.

Sincerely,

{See appended electronic signature page}

Sumathi Nambiar, M.D., M.P.H.
Acting Director
Division of Anti-Infective Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research

ENCLOSURE(S):
Content of Labeling

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

SUMATHI NAMBIAR
08/14/2013