

**CENTER FOR DRUG EVALUATION AND RESEARCH**

**Approval Package for:**

***APPLICATION NUMBER:***

**020634Orig1s061, 020635Orig1s067,  
021721Orig1s028**

***Trade Name:*** Levaquin Tablets, Levaquin Injection, Levaquin Oral Solution

***Generic Name:*** levofloxacin

***Sponsor:*** Janssen Pharmaceuticals, Inc.

***Approval Date:*** April 27, 2012

***Indications:*** For treatment and prophylaxis of plague due to *Yersinia pestis* in adults and pediatric patients 6 months of age and older.

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021721Orig1s028**

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**APPROVAL LETTER**



NDA 020634/S-061  
NDA 020635/S-067  
NDA 021721/S-028

**sNDA APPROVAL – ANIMAL EFFICACY**

Janssen Pharmaceuticals, Inc.  
c/o Johnson & Johnson Pharmaceutical Research and Development, LLC  
Attention: Melissa L. Gannon  
Director, Regulatory Affairs  
920 Route 202 South, PO Box 300  
Raritan, NJ 08869-0602

Dear Ms. Gannon:

Please refer to your Supplemental New Drug Applications (sNDAs) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for the following:

<b>NDA #</b>	<b>Supplement number</b>	<b>Drug Name &amp; Dosage Form</b>	<b>Letter Date</b>	<b>Receipt Date</b>
020634	S-061	Levaquin (levofloxacin) Tablets, 250 mg, 500 mg, 750 mg	October 27, 2011	October 28, 2011
020635	S-067	Levaquin (levofloxacin) Injection	November 4, 2011	November 7, 2011
021721	S-028	Levaquin (levofloxacin) Oral Solution	November 4, 2011	November 7, 2011

We acknowledge receipt of your amendments dated November 23, December 21, 22 and 23, 2011, January 12, February 6 and 23, March 5, 12 and 30, and April 25 and 26, 2012.

These “Prior Approval” supplemental new drug applications propose to add to the label the indication for treatment and prophylaxis of plague due to *Yersinia pestis* in adults and pediatric patients 6 months of age and older.

We have completed our review of these supplemental applications, as amended. They are approved, under the provisions of 21 CFR 314, Subpart I (Approval of New Drugs When Human Efficacy Studies Are Not Ethical or Feasible), effective on the date of this letter, for use as recommended in the enclosed, agreed-upon labeling text and required patient labeling. Marketing of these drug products and related activities must adhere to the substance and procedures of the referenced animal efficacy regulations.

### **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, text for the 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 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 includes 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).

### **CARTON AND IMMEDIATE CONTAINER LABELS**

We acknowledge your October 27, 2011, and November 4, 2011, submissions containing final printed carton and container labels.

## **SUBPART I APPROVAL REQUIREMENTS**

Approvals under 21 CFR Part 314, Subpart I (Approval of New Drugs When Human Efficacy Studies Are Not Ethical or Feasible) are subject to three requirements:

1. *Approval with restrictions to ensure safe use.* This subsection permits the Agency to require postmarketing restrictions as are needed to ensure safe use of the drug product, commensurate with the specific safety concerns presented by the drug product. We conclude that levofloxacin can be safely used without restrictions on distribution or use.
2. *Information to be provided to patient recipients.* This subsection requires applicants to prepare labeling to be provided to patient recipients for drug products approved under this subpart. We conclude that the FDA-Approved Medication Guide for LEVAQUIN meets the requirements of this subsection. We remind you that the medication guide must be available with the product to be provided, when possible, prior to administration or dispensing of the drug product for the use approved under this subpart.
3. *Postmarketing Studies.* This subsection requires you to conduct postmarketing studies, such as field studies, to verify and describe the drug's clinical benefit and to assess its safety when used as indicated when such studies are feasible and ethical. We refer to your letter dated April 25, 2012, stating that you agree to conduct a field study to evaluate the efficacy and safety of LEVAQUIN in the event of an attack with intentional release of *Yersinia pestis* in the United States and to submit a protocol for the field study on or before April 30, 2013.

## **POSTMARKETING REQUIREMENT**

We remind you of your postmarketing requirement specified in your submission dated April 25, 2012. The requirement is listed below.

1893-001 To conduct a field study to evaluate the efficacy and safety of levofloxacin in the event of an attack with the intentional release of *Yersinia pestis* in the United States

Final Protocol Submission: 04/13  
Study/Trial Completion: To be determined should an event occur  
Final Report Submission: To be determined should an event occur

Submit your clinical protocol to IND 036627 and IND 038368. Submit final reports to the NDAs as supplemental applications. For administrative purposes, all submissions relating to this postmarketing requirement must be clearly designated "**Subpart I Postmarketing Requirements.**"

### **REQUIRED PEDIATRIC ASSESSMENTS**

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication(s) in pediatric patients unless this requirement is waived, deferred, or inapplicable.

We are waiving the pediatric study requirement for pediatric patients less than 6 months of age because necessary studies are impossible or highly impracticable.

This product is appropriately labeled for use in pediatric patients 6 months of age and older for this indication. Therefore, no additional studies are needed in this pediatric group.

### **PROMOTIONAL MATERIALS**

Immediately submit all promotional materials (both promotional labeling and advertisements) to be used within the first 120 days after approval. Send one copy to the Division of Anti-Infective Products and two copies of the promotional materials and the package insert directly to:

Food and Drug Administration  
Center for Drug Evaluation and Research  
Division of Drug Marketing, Advertising, and Communications  
5901-B Ammendale Road  
Beltsville, MD 20705-1266

In addition, as required by 21 CFR 314.640, submit all subsequent promotional materials at least 30 days before the intended time of initial distribution of labeling or initial publication of the advertisement. Send two copies of the promotional materials and the package insert to the address above.

**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 Jane A. Dean, RN, MSN, Regulatory Health Project Manager, at (301) 796-1202.

Sincerely,

*{See appended electronic signature page}*

Katherine Laessig, MD  
Deputy Director  
Division of Anti-Infective Products  
Office of Antimicrobial Products  
Center for Drug Evaluation and Research

ENCLOSURE(S):  
Content of Labeling

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**This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.**  
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/s/  
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KATHERINE A LAESSIG  
04/27/2012