

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*

**21-721**

**PHARMACOLOGY REVIEW(S)**

## PHARMACOLOGY/TOXICOLOGY REVIEW AND EVALUATION

NDA Number: 21-721  
Serial Number: 000  
Date Received: 12/19/03  
Product: Levaquin® (levofloxacin) Oral Solution  
Clinical Population: Adults (Men and Women)  
Sponsor: Johnson and Johnson Pharmaceutical Research and  
Development, LLC

Review Division: Special Pathogen and Immunologic Drug Products  
(HFD-590)

Reviewer: Stephen G. Hundley, Ph.D., DABT  
Pharmacology/Toxicology Reviewer

Supervisor: Steve Gitterman, M.D., Ph.D.  
Deputy Division Director

Division Director: Renata Albrecht, M.D.

Project Manager: Rebecca Saville

Review Submission Date: 10/11/04

**EXECUTIVE SUMMARY****Recommendations:**

**Approvability** – The NDA submission is approvable from the perspective of nonclinical pharmacology and toxicology.

**Nonclinical Studies** – Additional nonclinical studies are not required.

**Labeling** – The sponsor's proposed label is acceptable with regard to the nonclinical pharmacology and toxicology portions of the label.

**Summary of Nonclinical Findings:**

Nonclinical pharmacology and toxicology studies were previously submitted under NDA's 20-364 & 20-635 and were sufficient for the following LEVAQUIN® indications: acute sinusitis, acute bacterial exacerbation of chronic bronchitis, community-acquired pneumonia, complicated skin and skin structure infections, uncomplicated skin and skin structure infections, complicated urinary tract infections, uncomplicated urinary tract infections, and acute pyelonephritis. The previously submitted nonclinical data base supports the LEVAQUIN® (levofloxacin) Oral Solution formulation. Therefore, additional nonclinical pharmacology and toxicology studies were not required.

No additional Pharmacology/Toxicology NDA Review is provided beyond the Cover Sheet, Executive Summary, and Drug Information.

**APPEARS THIS WAY  
ON ORIGINAL**

**DRUG INFORMATION**

**NDA:** 21-721  
**Type of Indication:** Original  
**Review Number:** 1  
**Date of Submission:** 12/19/03  
**Information to Sponsor:** Yes ( ) No (X)

**Sponsor/Manufacturer:**

Johnson & Johnson Pharmaceutical Research & Development, L.L.C.  
920 Route 202 South, P.O. Box 300  
Raritan, NJ 08869

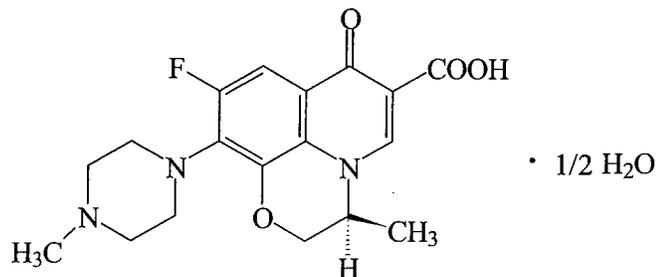
**Reviewer:** Stephen G. Hundley, Ph.D., DABT  
Pharmacology/Toxicology Reviewer

**Review Division:** Special Pathogen and Immunologic Drug Products  
HFD-590

**Review Completion Date:** 10/11/04

**Drug Information:**

**Generic Name:** Levofloxacin  
**Drug Product:** LEVAQUIN® Tablet & IV (NDA's 20-634 & 20-635)  
**Chemical Name:** S-(-)-9-Fluoro-2,3-dihydro-3-methyl-10-(4-methyl-1-piperazinyl) -7-oxo-7H-pyrido [1,2,3-de] 1,4-benzoxazine-6-carboxylic acid hemihydrate  
**CAS #:** 100986-85-4  
**Molecular Formula:** C<sub>18</sub>H<sub>20</sub>FN<sub>3</sub>O<sub>4</sub> · ½ H<sub>2</sub>O  
**Molecular Weight:** 370.4  
**Molecular Structure:**



**Related Submissions:** IND's 36,627 & 38,368; NDA's 20-635 & 20-635

**Drug Class:** Antimicrobial (Fluoroquinolone)

**Intended Population:** Adults

**Current Indications:** Acute Sinusitis, Acute Bacterial Exacerbation of Chronic Bronchitis, Community Acquired Pneumonia, Nosocomial Pneumonia, Uncomplicated Urinary Tract Infection, Complicated Urinary Tract Infection, Acute Pyelonephritis, Uncomplicated Skin and Skin Structure Infection, Complicated Skin and Skin Structure Infection, Bacterial Prostatitis

**Clinical Formualtion:** LEVAQUIN® (levofloxacin) Oral Solution, 25 mg/ml

**Route of Administration:** Oral

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Stephen G. Hundley, Ph.D., DABT  
Acting Team Leader & Pharmacology/Toxicology Reviewer  
Division of Special Pathogen and Immunologic Drug Products  
HFD-590

Concurrence:

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Steve Gitterman, MD  
Deputy Division Director  
Division of Special Pathogen and Immunologic Drug Products  
HFD-590

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/s/

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Steve Hundley  
10/18/04 03:49:41 PM  
PHARMACOLOGIST

Renata Albrecht  
10/19/04 03:22:50 PM  
MEDICAL OFFICER