

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*

**21-721**

**MICROBIOLOGY REVIEW(S)**

**MICROBIOLOGY REVIEW**  
**DIVISION OF SPECIAL PATHOGEN AND IMMUNOLOGIC DRUG PRODUCTS**  
**(HFD-590)**

**NDA #:** 21-721

**REVIEWER:** Peter A. Dionne  
**CORRESPONDENCE DATE:** 19-DEC-03  
**CDER DATE:** 19-DEC-03  
**REVIEW ASSIGN DATE:** 15-DEC-03  
**REVIEW COMPLETE DATE:** 21-JAN-04

**SPONSOR:** Johnson & Johnson Pharmaceutical Research and Development L.L.C.  
920 U.S. Highway 202  
P.O. Box 300  
Raritan, New Jersey 08869-0602

**CONTACT PERSON:** Manisha Padhye, Ph.D.  
Associate Director, Regulatory Affairs  
Phone Number: (908) 704-4600

**SUBMISSION REVIEWED:** Original NDA for oral solution

**DRUG CATEGORY:** Antimicrobial: Fluoroquinolone

**INDICATIONS:** Community acquired pneumonia, acute bacterial exacerbations of chronic bronchitis, acute bacterial sinusitis, uncomplicated and complicated skin and soft tissue infections, uncomplicated and complicated urinary tract infections and acute pyelonephritis.

**DOSAGE FORM:** 25mg/mL—oral solution

**DRUG PRODUCT NAME**

**PROPRIETARY:**

LEVAQUIN™ Oral Solution

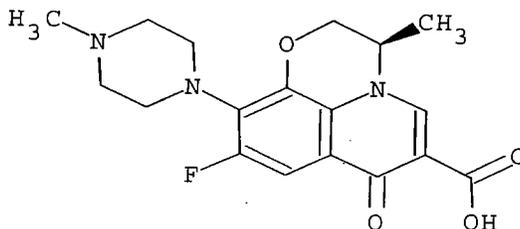
**NONPROPRIETARY/USAN:**

Levofloxacin oral solution

**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

**STRUCTURAL FORMULA:**



**Molecular Formula:** C<sub>18</sub>H<sub>20</sub>FN<sub>3</sub>O<sub>4</sub>

**Molecular Weight:** 361.38

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**Levofloxacin Oral Solution**

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**SUPPORTING DOCUMENTS:**

IND 38,368—Levofloxacin Injection

IND 36,627—Levofloxacin Tablets

NDA 20-634—Levofloxacin Tablets—approved 12/20/1996

NDA 20-635—Levofloxacin Injection—approved 12/20/1996

**BACKGROUND:**

This is a new drug application to provide for the use of a new oral solution formulation of levofloxacin. This new oral solution has been developed for use in the treatment of all approved indications for levofloxacin tablets and injections.

The application consists of a CMC (chemistry and manufacturing controls) section for the new formulation, study reports for two bioavailability and comparative bioequivalence studies, and study reports for two taste test studies.

Study LOFBO-PHI-116 was an open-label, randomized, single-dose, 3-way crossover study that was used to assess the bioequivalence of an oral formulation of levofloxacin, an oral solution formulation of levofloxacin, and the 500 mg marketed tablet, with the tablet formulation as the reference. Seventy-two subjects took part in this study.

Study LOFBO-PHI-117 was an open-label, randomized, single-dose, 2-way crossover study to evaluate the effect of food on the pharmacokinetics of an oral solution of levofloxacin. Twenty-four subjects were used in this study.

Study LOFBO-LSTT-002 was an open-label, randomized, 6-sequence, 6-period, crossover study to compare the overall taste and palatability of 6 varying flavored levofloxacin oral formulations. One hundred and twenty subjects took part in this study.

Study LOFBO-LSTT-003 was a single-blind, randomized, 2-sequence, 2-period, crossover study to compare the overall taste and palatability of 2 flavored levofloxacin oral formulations (tablets and solution). Seventy-six subjects were used in the study.

There is no microbiology involved in these studies or in this new application.

The microbiology section of the package insert is identical to that in the present approved labeling.

**CONCLUSIONS & RECOMMENDATIONS:**

Since this application involves no microbiology it should be approved from the microbiology viewpoint.

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Levofloxacin Oral Solution**

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ON ORIGINAL**

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Peter A. Dionne  
Microbiologist HFD-590

**CONCURRENCES:**

HFD-590/Div Dir _____	Signature _____	Date _____
HFD-590/TLMicro _____	Signature _____	Date _____

**CC:**  
HFD-590/Original NDA # 21-721  
HFD-590/Division File  
HFD-590/Micro/PDionne  
HFD-590/MO/SJang  
HFD-520/Pharm/SHundley  
HFD-590/Chem/GHolbert  
HFD-590/CSO/SPeacock

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/s/

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Peter Dionne  
2/2/04 02:36:15 PM  
MICROBIOLOGIST

Shukal signed 1/16/04--Steve signed 1/30/04

Shukal Bala  
2/5/04 07:57:16 AM  
MICROBIOLOGIST

Steve Hundley  
2/5/04 12:28:30 PM  
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