CLINICAL PHARMACOLOGY REVIEW

NDA: 20-634 S043 (Tablets); 20-635 S046 (Injection); 21-721 S011 (Oral Solution)	Submission Date(s): December 20, 2006
Brand Name	Levaquin®
Generic Name	Levofloxacin
Reviewer	Seong H. Jang, Ph.D.
Team Leader	Phil M. Colangelo, Pharm.D., Ph.D.
OCP Division	DCP4
OND Division	DSPTP
Sponsor	Johnson & Johnson
Submission Type; Code	Pediatric Study Report; SE5
Formulation; Strength(s)	Tablets: 250 mg, 500 mg and 750 mg Oral Solution: 25 mg/mL Single dose Injection: 500 mg in 20 mL; and 750 mg in 30 mL Levaquin in 5% Dextrose Injection: 250 mg in 50 mL; 500 mg in 100 mL; and 750 mg in 150 mL
Proposed Indications	None; Adding pediatric safety and PK information
Dosage and Administration	Not Applicable

Levofloxacin (Levaquin®) Tablets, Injection and Oral Solution are approved products for the treatment of adults (≥ 18 years of age) with acute bacterial sinusitis, acute bacterial exacerbation of chronic bronchitis, nosocomial pneumonia, community-acquired pneumonia, complicated skin and skin structure infections, uncomplicated skin and skin structure infections, chronic bacterial prostatitis, complicated urinary tract infections, acute pyelonephritis, uncomplicated urinary tract infections caused by susceptible strains of designated microorganisms, and prevention of inhalational anthrax, post-exposure as listed in the final product labeling.

The sponsor submitted these supplemental NDAs for Levaquin® (levofloxacin) Tablets, Injection, and Oral Solution to fulfill the requirements of the Written Request for Pediatric Studies, which FDA originally issued on December 2001 and then in its final, amended form on June 16, 2006. The supplements currently submitted provide efficacy and safety data in the treatment of pediatric community-acquired pneumonia (PCAP; Study LOFBIV-PCAP-003) and acute otitis media (AOM; Studies LOFBO-OTMD-001 and LOFBO-OTMD-002), and the long-term (1 year) safety data from children who participated in the PCAP and AOM trials (Study LFOBO-LTSS-001) in the fulfillment of the Written Request. -- ---------- ---------- - ---------- ------ --------- ------- - -- ------ ------ --------- ------ ------ ---------- ----- ---------- --------- ---------- ---------- ---------- --- ---------- -- ---------- - - -- - -------- ---------- ---------- -------- --- -------- ---------. The indication of prevention of inhalational anthrax, post-exposure was approved only for adults, as it was deemed by the Division of Special Pathogen a--- Transplant Products that additional safety data was needed for pediatric patients. ----- ---------- ---------- ---------- ---------- --------- --------- ----------

The sponsor does not wish to pursue a pediatric indication for Levaquin® for either CAP or AOM in these current supplemental NDAs. Thus, no Clinical Pharmacology / Pharmacokinetic information for levofloxacin in pediatric patients will be included in the proposed labeling for these supplemental NDAs.

The review of Clinical Pharmacology information provided in the Phase 3 PCAP study (LOFBIV-PCAP-003) showed that the systemic exposure (i.e., AUC) following the dosage regimens evaluated (i.e., 10 mg/kg BID for children <5 years of age and 10 mg/kg QD for children ≥5 years of age) did not adequately match up to the exposure in adults when given the approved dosage regimen of 500 mg QD. [redacted]

Seong H. Jang, Ph.D.
Reviewer
Clinical Pharmacology
DCP4/OCP/OTS

Concurrence

Phil Colangelo, Pharm.D., Ph.D.
Team Leader
Clinical Pharmacology
DCP4/OCP/OTS

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/s/

Seong Jang
6/8/2007 09:53:22 AM
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Phil Colangelo
6/12/2007 02:15:36 PM
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