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APPROVAL PACKAGE FOR:

APPLICATION NUMBER

21-554

Pharmacology Review(s)

PHARMACOLOGY/TOXICOLOGY COVER SHEET

NDA: 21-554
Review Number: 1
Date of Submission: 10/29/02
Information to Sponsor: Yes () No (X)

Sponsor: Bayer Corporation
400 Morgan Lane
West Haven, CT 06516-4175

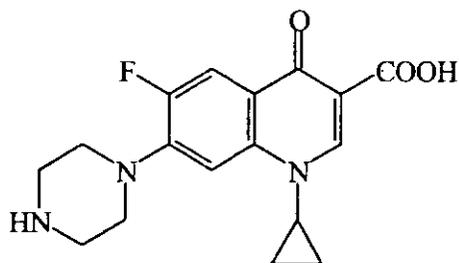
Manufacturer of Drug Substance:
Bayer AG
D-51368 Leverkusen
Germany

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

Division: Special Pathogen and Immunologic Drug Products
HFD-590

Review Completion Date: 3/3/03

Drug Product: Cipro XR (1000 mg tablet)
Generic Name: Cipro®
Code Name: Not Applicable
Drug Substance: Ciprofloxacin HCl and Ciprofloxacin betaine (base)
Chemical Name: 1-Cyclopropyl-6-fluoro-1,4-dihydro-4-oxo-7[1-piperazinyl]-3-quinoline-carboxylic acid
CAS#: 85721-33-1
Molecular Formula: C₁₇H₁₈FN₃O₃
Molecular Weight: 331.4 (385.8 for the monochloride monohydrate salt)
Molecular Structure:



Relevant IND: 61,331

Drug Class: Antimicrobial Fluoroquinolone

Indication: Complicated Urinary Tract Infection and Acute Uncomplicated Pyelonephritis

Clinical Formulation: Extended Release Tablet

Route of Administration: Oral

Proposed Use: Single 1000 mg Cipro XR tablet daily for 7 to 14 consecutive days.

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:

Previously submitted nonclinical studies supported the approval of ciprofloxacin (CIPRO®) for several indications under NDA's 19-537, 20-780, 19-857, 19-858, and 19-847. Included in the approved indications are acute sinusitis, acute exacerbation of chronic bronchitis, bacterial prostatitis, skin and skin structure infections, bone and joint infections, complicated intra-abdominal infections, and lower respiratory tract infections. Critical evaluation of previously submitted nonclinical toxicology studies with ciprofloxacin supported the conduct of clinical trials for complicated bone and joint infections where the dosing regimen was 750 mg ciprofloxacin b.i.d., for a period up to six weeks. The same nonclinical data base is more than sufficient to support the current indication for treatment of complicated urinary tract infection and acute uncomplicated pyelonephritis with Cipro XR at a 1000 mg daily dose of ciprofloxacin for a period of 7 to 14 days.

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

/S/

Stephen G. Hundley, Ph.D., DABT
Pharmacology/Toxicology Reviewer
Division of Special Pathogen and Immunologic Drug Products (HFD-590)

Concurrence:

/S/

Kenneth Hastings, Dr. P.H., DABT
Pharmacology/Toxicology Supervisor & Team Leader
Division of Special Pathogen and Immunologic Drug Products (HFD-590)

cc:

HFD-590/CSO/S. Peacock
HFD-590/MO/M. Ruiz
HFD-590/MO/R. Roca
HFD-590/Biopharm/D. Chilukuri
HFD-590/Micro/P. Dionne
HFD-590/Chem/D. Matecka

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/s/

Steve Hundley
3/5/03 11:45:53 AM
PHARMACOLOGIST

Kenneth Hastings
3/5/03 12:48:42 PM
PHARMACOLOGIST

Renata Albrecht
3/29/03 09:08:16 AM
MEDICAL OFFICER