

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

19-537/S-015

APPROVAL LETTER

NDA 19-537/S-013
S-015

JUL 21 1994

Mr. Carl E. Calcagni
Director
Regulatory Affairs
Miles Inc.
Pharmaceutical Division
200 Morgan Lane
West Haven, CT 06516

Dear Mr. Calcagni:

Reference is made to your supplemental new drug applications (NDA's), S-013 dated October 22, 1991, and S-015 dated October 23, 1991, submitted pursuant to section 505(b) of the Federal Food, Drug, and Cosmetic Act for CIPRO® (ciprofloxacin hydrochloride) Tablets, providing for the addition of uncomplicated gonorrhea (S-013) and typhoid fever (S-015) to the **INDICATIONS AND USAGE** section of the labeling.

We also acknowledge receipt of your additional communication dated June 9, 1994, providing for final printed labeling (FPL). We have completed our review of FPL "PZ100779" dated June 1994, and it is approved as of the date of this letter. However, we request that at the next FPL printing you make the revisions below.

1. Under the **DOSAGE AND ADMINISTRATION** section, the third paragraph, "Infectious Diarrhea" and "Typhoid Fever" should be written in lower case. Also, in the sixth paragraph, fifth sentence, the word "diarrhea" should be written in lower case.
2. Under the **ADVERSE REACTIONS** section, the last paragraph, please move pseudomembranous colitis to the end of the list of adverse reactions and add the following sentence: "The onset of pseudomembranous colitis symptoms may occur during or after antimicrobial treatment."

This approval affects only those changes specifically submitted in these supplemental applications. Other changes which may be approved or are pending are not affected.

Should additional information relating to the safety and effectiveness of this drug product become available, further revision of the labeling may be required.

We remind you that you must comply with the requirements set forth under 21 CFR 314.80 and 314.81 for an approved NDA.

Should you have any questions concerning this issue, please contact Ms. Pauline Fogarty, of the Project Management Staff, at 301-443-6797.

Sincerely yours,

Lillian Gavrilovich, M.D.
Acting Director
Division of Anti-Infective Drug Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

CC:Orig NDA 19-537

HFD-130

HFD-82

HFD-500

HFD-638

HFD-735

HFD-520

HFD-520/MO/MBlum

HFD-520/Pharm/Buko

HFD-520/Chem/Shetty

HFD-520/Micro/PDionne

HFD-521/PM/PFogarty

fogarty7/20/94

APPROVAL

Concurrence:

HFD-520/ActDivDir/LGavrilovich

HFD-520/SMO/MAlbuerne

HFD-521/APM/PDeSantis

IS 7/21/94

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CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

19-537/S-015

APPROVABLE LETTER

201

NDA 19-537/S-015

Mr. Carl E. Calcagni
Director
Regulatory Affairs
Miles Inc.
Pharmaceutical Division
200 Morgan Lane
West Haven, CT 06516

APR 16 1993

Dear Mr. Calcagni:

Reference is made to your supplemental New Drug Application (NDA) dated October 23, 1991, submitted pursuant to section 505(b) of the Federal Food, Drug, and Cosmetic Act for Cipro® (ciprofloxacin hydrochloride) Tablets, providing for the addition of typhoid fever to the INDICATIONS AND USAGE section of the labeling.

We have completed our review of this supplement, and it is approvable. However, before it may be approved, we request that you make the labeling changes listed below:

CLINICAL PHARMACOLOGY:

Please revise the Microbiology subsection so that only *Salmonella typhi* is added to the listing of Gram-negative bacteria for which activity has been shown both *in vitro* and in clinical infections.

INDICATIONS AND USAGE:

Please add the following:

"Typhoid Fever (enteric fever) caused by *Salmonella typhi*."

" NOTE: The efficacy of ciprofloxacin in the eradication of the chronic typhoid carrier state has not been demonstrated."

DOSAGE AND ADMINISTRATION:

1. Please revise the third paragraph to read: "The recommended adult dosage for infectious diarrhea, and typhoid fever is 500 mg every 12 hours."

2. Under the chart labeled "DOSAGE GUIDELINES", please revise the name of the first heading, and add the following sentence:

<u>Type of Infection</u>	<u>Type or Severity</u>	<u>Unit Dose</u>	<u>Frequency</u>	<u>Daily Dose</u>
Typhoid Fever	Mild/Moderate	500 mg	q 12 h	1000 mg

3. Please add to the paragraph which begins, "The duration of treatment depends upon..."., the sentence: "Typhoid fever should be treated for 10 days". This new sentence should become the last sentence of that paragraph.

Please submit twelve copies of final printed labeling (FPL) with the above changes. Should additional information relating to the safety and effectiveness of this drug product become available, further revision of the labeling may be required.

Within 10 days after the date of this letter, you are required to amend the supplemental application, notify us of your intent to file an amendment, or follow one of the other alternatives under 21 CFR 314.110. In the absence of such action, the Food and Drug Administration may take action to withdraw the supplemental application.

Should you have any questions concerning this issue, please contact Ms. Pauline Fogarty, of the Project Management Staff, at 301-443-6797.

Sincerely yours,

MS/ 4/15/93

Murray M. Lumpkin, M.D.
Director
Division of Anti-Infective Drug Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

CC:Orig NDA 19-537
HFD-130
HFD-82
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HFD-520
HFD-520/DivDir/MLumpkin
HFD-520/MO/PCoyne
HFD-520/Pharm/LBuko
HFD-520/Chem/VShetty
HFD-520/Micro/PDionne
HFD-521/PMS/PFogarty *4/15/93*
fogarty4/6/93;4/15/93
APPROVABLE

Concurrence only:
HFD-520/SMO/RAlbrecht

HFD-520/SMO/MALBERNE MS/ 4/15/93

HFD-521/SPMS/JBones

MS/ 4/15/93