

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

19-537/S038

19-847/S024

19-857/S027

19-858/S021

20-780/S008

APPROVAL LETTER



DEPARTMENT OF HEALTH & HUMAN SERVICES

HFD-590 / V. Jensen

Food and Drug Administration
Rockville MD 20857

NDA 19-537/S-038
NDA 19-847/S-024
NDA 19-857/S-027
NDA 19-858/S-021
NDA 20-780/S-008

AUG 30 2000

Bayer Corporation
Pharmaceutical Division
Attention: Andrew S. Verderame
Associate Director, Regulatory Affairs
400 Morgan Lane
West Haven, CT 06416-4175

Dear Mr. Verderame:

Please refer to your supplemental new drug application, NDA 19-537/S-038, dated February 29, 2000, received March 1, 2000, and your supplemental new drug applications, NDAs 19-847/S-024, 19-857/S-027, 19-858/S-021, and 20-780/S-008, dated February 29, 2000, and received March 2, 2000, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for CIPRO[®] (ciprofloxacin hydrochloride) Tablets, IV Solution, IV in 5% Dextrose, IV in 0.9% Saline, and Oral Suspension, respectively.

We acknowledge receipt of your submissions dated June 20, June 30, and August 29, 2000 (2).

These supplements provide for the use of CIPRO[®] for inhalational anthrax (post-exposure).

We have completed the review of these supplemental applications, as amended, according to the regulations for accelerated approval, and have concluded that adequate information has been presented to approve CIPRO[®] (ciprofloxacin hydrochloride) Tablets, IV Solution, IV in 5% Dextrose, IV in 0.9% Saline, and Oral Suspension for use as recommended in the agreed upon labeling dated August 29, 2000. Accordingly, these supplemental applications are approved under 21 CFR 314 Subpart H. Approval is effective on the date of this letter. Marketing of these drug products and related activities for the indication of inhalational anthrax (post-exposure) are to be in accordance with the substance and procedures of the referenced accelerated approval regulations.

The final printed labeling (FPL) must be identical to the submitted labeling (text for the oral formulations package insert and text for the IV formulations package insert submitted August 29, 2000).

Please submit 20 paper copies of the FPL as soon as they are available, in no case more than 30 days after they are printed, to each application. Please individually mount ten of the copies on —

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heavy-weight paper or similar material. Alternatively, you may submit the FPL electronically according to the guidance for industry titled *Providing Regulatory Submissions in Electronic*

Format - NDAs (January 1999). For administrative purposes, these submissions should be designated "FPL for approved supplements NDA 19-537/S-038, 20-780/S-008" and "FPL for approved supplements NDA, 19-847/S-024, 19-857/S-027, 19-858/S-021." Approval of these submissions by FDA is not required before the labeling is used.

Products approved under the accelerated approval regulations, 21 CFR 314.510, require further studies to verify and describe clinical benefit. We remind you of your post-marketing study (Subpart H, Phase 4 commitment) specified in your submission dated August 29, 2000. This commitment is:

To cooperate with U.S.-based public health agencies in evaluating data on the use of CIPRO[®] brand of ciprofloxacin in a large U.S. population for inhalational anthrax (post-exposure), should an exposure occur.

Reports should be submitted to these NDAs as supplemental applications. For administrative purposes, all submissions relating to this Phase 4 commitment must be clearly designated "Subpart H, Phase 4 Commitments."

We also remind you that, under 21 CFR 314.550, after the initial 120 day period following the approval of the indication of inhalational anthrax (post-exposure), you must submit all promotional materials for the indication of inhalational anthrax (post-exposure), including promotional labeling as well as advertisements, at least 30 days prior to the intended time of initial dissemination of the labeling or initial publication of the advertisement.

Be advised that, as of April 1, 1999, all applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred (63 FR 66632). We note the pediatric data submitted with these supplements and defer submission of the above-mentioned pediatric requirement for the indication of inhalational anthrax (post-exposure) until January 1, 2004. This submission would consist of the initial study report from your long-term pediatric observational study, as specified in our May 12, 1999 Written Request letter.

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

If you have any questions, call Valerie Jensen, R.Ph., Regulatory Project Manager, at (301) 827-2127.

Sincerely,

A handwritten signature in black ink, appearing to read "D. Murphy, M.D.", written in a cursive style.

Dianne Murphy, M.D.

Director

Office of Drug Evaluation IV

Center for Drug Evaluation and Research

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cc:

Archival NDAs 19-537,
19-847, 19-857, 19-858, 20-780
HFD-590/Div. Files
HFD-590/V.Jensen
HF-2/MedWatch (with labeling)
HFD-002/ORM (with labeling)
HFD-095/DDMS-IMT (with labeling)
HFD-104/ADRA (with labeling)
HFI-20/Press Office (with labeling)
HFD-42/DDMAC (with labeling)
HFD-104/Peds/V.Kao (with labeling)
HFD-104/Peds/T.Crescenzi (with labeling)
HFD-400/OPDRA (with labeling)
HFD-613/OGD (with labeling)
HFD-21/ACS (with labeling)
HFD-830/DNDC Division Director
DISTRICT OFFICE
HFD-102/Cobbs

Drafted by: vj/August 9, 2000

Initialed by:

final:

filename: subparth

APPROVAL under Subpart H (AP) (Subpart H Phase 4 Commitments)

Concurrence:

HFD-590/Renata Albrecht/Acting Division Director @ 8/30/00
HFD-520/Gary Chikami/Division Director
HFD-590/Rigoberto Roca/Medical Team Leader *RRK 8/30/00*
HFD-590/Andrea Meyerhoff/Medical Reviewer *AMM 8/30/00*
HFD-590/Funmi Ajayi/Biopharm Team Leader
HFD-590/Joette Meyer/Biopharm Reviewer
HFD-725/Karen Higgins/Statistical TL
HFD-590/Kenneth Hastings/Pharm-tox TL
HFD-725/M. Huque/Dir DOB III
HFD-530/James Farrelly/Assoc. Dir. Pharm-tox
HFD-880/J. Lazor/Dir DPE III
HFD-590/Ellen Frank/CPMS *ef 8-30-00*
HFD-520/Terry Peters/Pharm-tox Reviewer
HFD-590/Shukal Bala/Acting Microbiology TL
HFD-590/Peter Dionne/Microbiology Reviewer
HFD-590/Stephen Hundley/Pharm-tox Reviewer
HFD-590/Norman Schmuff/Chemistry TL
HFD-590/Dorota Matecka/Chemistry Reviewer
HFD-104/Rosemary Roberts/PDIT/MO
HFD-104/Terrie Crescenzi/PDIT/PM
ODEIV/David Roeder/Acting Director, *DR 8-30-00*
Regulatory Affairs