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APPLICATION NUMBER:

21-085

APPROVAL LETTER

NDA 21-085

Bayer Corporation
Pharmaceutical Division
Attention: Andrew Verderame
Associate Director, Regulatory Affairs
400 Morgan Lane
West Haven, CT 06516-4175

Dear Mr. Verderame:

Please refer to your new drug application (NDA) dated December 9, 1998, received December 10, 1998, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Avelox™ (moxifloxacin hydrochloride) tablets, 400mg.

We acknowledge receipt of your submissions dated as follows:

February 11, 1999	September 3, 1999	October 12, 1999
February 23, 1999	September 8, 1999(2)	October 22, 1999
April 12, 1999	September 21, 1999	October 25, 1999(2)
April 22, 1999	September 27, 1999	November 19, 1999
June 14, 1999	September 29, 1999	December 8, 1999
July 8, 1999	September 30, 1999(2)	December 10, 1999
July 9, 1999	October 11, 1999	

This new drug application provides for the use of Avelox™ (moxifloxacin hydrochloride) tablets for acute bacterial sinusitis, acute bacterial exacerbation of chronic bronchitis, community-acquired pneumonia, as well as [ ].

We have completed the review of this application, as amended. We have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the agreed upon labeling submitted December 10, 1999 for acute bacterial sinusitis, acute bacterial exacerbation of chronic bronchitis, and mild to moderate community-acquired pneumonia. Accordingly, the application is approved for these indications, effective on the date of this letter.

In addition, we have concluded that the indication of [ ] is approvable pending submission of post-marketing data confirming the safety of moxifloxacin and therefore demonstrating an acceptable risk benefit profile. These data will be obtained from completion of Phase 4 commitments 1,2,4,5 and 6 listed below.

[

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The Division anticipates discussing the details of the above studies at your earliest convenience.

The Phase 4 commitments to which Bayer Corporation (Bayer) agreed in its submission dated December 10, 1999, along with any completion dates agreed upon, are listed below:

1. To better understand the risk/benefit profile of oral moxifloxacin tablets, Bayer will review post-marketing adverse event data following at least one million patient exposures worldwide. A substantial proportion of these exposures will be from the United States. The results of this evaluation will be submitted to the Division by September 30, 2000.

2. Bayer will conduct and submit the results of its active surveillance program currently being conducted in Germany or other foreign countries where active surveillance programs currently exist. The results of this program will provide information on incidence of adverse events using moxifloxacin tablets for at least 15,000 moxifloxacin exposures. Please submit protocols and methods for this ongoing study to the Division within ninety days of receipt of this letter. A report on this experience will be submitted to the Division by September 30, 2000.

3. Bayer will conduct and submit the results of an active surveillance program in the United States similar to the ongoing moxifloxacin active adverse event surveillance program in Germany. The results of this program should provide information on incidence of adverse events using moxifloxacin tablets for at least 15,000 moxifloxacin exposures. Before initiating this study, please submit the protocol and proposed methods within ninety days of receipt of this letter. The results of this study should be submitted to the Division by September 30, 2000.

4. Bayer will conduct a moxifloxacin single oral dose escalation study of the effects on QTc at Cmax. The results of this study will be submitted to the Division by December 31, 2000.

5. Bayer will conduct a comparison study of the effects of moxifloxacin, levofloxacin, and erythromycin on QTc at Cmax. The results of this study will be submitted to the Division by December 31, 2000.

6. Bayer will conduct a ten day multiple dose comparison study of moxifloxacin, sparfloxacin, and placebo effects on QTc at Cmax. The results of this study will be submitted to the Division by December 31, 2000.

7. Bayer will perform a study to characterize the pharmacokinetic profile of moxifloxacin and its conjugated metabolites (M1 and M2) in young and elderly adult males and females after single and multiple 400 mg oral doses. The results of this study will be submitted to the Division by December 31, 2000.

8. Bayer will re-evaluate the drug substance[ ] specifications after 2 years of commercial production for [ ].

The Division anticipates discussing the details of the above studies at your earliest convenience.

Protocols, data, and final reports for the Phase 4 commitments should be submitted to your IND for this product and a copy of the cover letter sent to this NDA. If an IND is not required to meet your Phase 4 commitments, please submit protocols, data and final reports to this NDA as correspondence. In addition, under 21 CFR 314.82(b)(2)(vii), we request that you include a status summary of each commitment in your annual report to this NDA. The status summary should include the number of patients entered in each study, expected completion and submission dates, and any changes in plans since the last annual report. For administrative purposes, all submissions, including labeling supplements, relating to these Phase 4 commitments must be clearly designated "Phase 4 Commitments."

The final printed labeling (FPL) must be identical to the submitted labeling dated December 10, 1999 (text for the package insert, immediate container and carton labels). Marketing the product with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

Please submit 20 copies of the FPL as soon as it is available, in no case more than 30 days after it is printed. Please individually mount ten of the copies on heavy-weight paper or similar material. For administrative purposes, this submission should be designated "FPL for approved NDA 21-085." Approval of this submission by FDA is not required before the labeling is used.

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 are waiving the pediatric study requirement for this action on this application.

In addition, please submit three copies of the introductory promotional materials that you propose to use for this product. All proposed materials should be submitted in draft or mock-up form, not final print. Please send one copy to the Division of Special Pathogen and Immunologic Drug Products and two copies of both the promotional materials and the package insert directly to:

Division of Drug Marketing, Advertising, and Communications, HFD-40
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857

Please submit one market package of the drug product when it is available.

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, contact Valerie Jensen, R.Ph., Regulatory Project Manager, at (301) 827-2127.

Acting Director
Center for Drug Evaluation and Research