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RESEARCH**

APPLICATION NUMBER:
21-334 *and* 21-085/S-010

APPROVAL LETTER



NDA 21-334
NDA 21-085/S-010

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

Dear Mr. Verderame:

Please refer to your new drug application (NDA 21-085) dated December 9, 1998, received December 10, 1998, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Avelox[®] (moxifloxacin HCl) Tablets, 400 mg.

Your submission of October 26, 2000, constituted a complete response to our December 10, 1999 action letter. The NDA number 21-334 was assigned to this submission for our administrative purposes.

We acknowledge receipt of your submissions dated as follows:

November 29, 2000	April 4, 2001	April 6, 2001	April 18, 2001
February 27, 2001	April 5, 2001	April 10, 2001	April 20, 2001

NDA 21-334 provides for the use of Avelox for the treatment of uncomplicated skin and skin structure infections.

Please also refer to your supplemental new drug application, (NDA 21-085/S-010) dated December 11, 2000, received December 12, 2000, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Avelox[®] (moxifloxacin HCl) Tablets, 400 mg.

We acknowledge receipt of your submissions dated as follows:

April 4, 2001	April 10, 2001	April 18, 2001
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This supplemental new drug application provides for revisions to the package insert to include the following safety information:

- Addition of a Post-Marketing Adverse Event Reports subsection in the **ADVERSE REACTIONS** section of the label. This subsection includes information about post-marketing adverse events including anaphylactic reaction and anaphylactic shock.
- Revisions to **PRECAUTIONS, Information for Patients** regarding information about hypersensitivity reactions including anaphylactic reactions.

We have completed the review of these applications, as amended, and 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 enclosed labeling text. Accordingly, these applications are approved effective on the date of this letter.

The final printed labeling (FPL) must be identical to the enclosed labeling (text for the package insert).

Please submit the copies of final printed labeling (FPL) electronically according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDA* (January 1999). Alternatively, you may submit 20 paper copies of the FPL as soon as it is available but no 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 21-334, NDA 21-085/S-010." 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 dererred (63 *FR* 66632). Please refer to our approval letter dated December 10, 1999 for NDA 21-085 in which the pediatric study requirement was waived.

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

Division of Drug Marketing, Advertising, and Communications, HFD-42
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857

Following submission of FPL and promotional materials, no further correspondence should be sent to NDA 21-334.

We have received your submissions dated September 18, 2000, September 19, 2000, September 28, 2000, October 3, 2000, and April 16, 2001 reporting on the following postmarketing study commitments:

1. Study 1
Results from a review of postmarketing adverse event data following at least one million patient exposures worldwide.

2. Study 2
Results of the active surveillance study in Germany involving at least 15,000 exposures to moxifloxacin.

3. Study 3
Results of the active surveillance program in the US involving at least 15,000 exposures to moxifloxacin.
4. Study 4
Results from a moxifloxacin single oral dose escalation study of the effects on QT_c at C_{max}.
5. Study 5
Results from a comparison study of the effects of moxifloxacin, levofloxacin, and erythromycin on QT_c at C_{max}.
6. Study 6
Results from a ten day multiple dose comparison study of moxifloxacin, sparfloxacin, and placebo effects on QT_c at C_{max}.
7. Study 7
Results from 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.
8. Study 8
Re-evaluate the drug substance impurity specifications after 2 years of commercial production for the following three impurities:

We have reviewed your submissions and conclude that the above commitments were fulfilled.

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81. Reports required should be sent to NDA 21-085.

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

Sincerely,

{See appended electronic signature page}

Mark J. Goldberger, M.D., M.P.H.
Director
Division of Special Pathogen and Immunologic Drug
Products
Office of Drug Evaluation IV
Center for Drug Evaluation and Research

Enclosure