DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 50-733/S-007

Pfizer Inc.
Attention: Rita Wittich
Vice President, Worldwide Regulatory Affairs
235 East 42nd Street
New York, NY 10017

Dear Ms. Wittich:

Please refer to your supplemental new drug application dated February 7, 2001, received February 8, 2001, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Zithromax® (azithromycin) IV.

This application is subject to the exemption provisions contained in section 125(d)(2) of Title I of the FDA Modernization Act of 1997.

We acknowledge receipt of your submission dated October 11, 2002.

This supplemental new drug application provides for the inclusion of results from drug-drug interaction studies in the package insert labeling.

We have completed our review of this application, as amended, and it is approved effective on the date of this letter, for use as recommended in the agreed-upon labeling text with the revisions listed below.

1. In the **CLINICAL PHARMACOLOGY** section, Pharmacokinetics subsection, 5th paragraph, add the parenthetical phrase "(two 250 mg capsules)" after the 8th word "azithromycin" to read:

   " Following single oral doses of 500 mg azithromycin (two 250 mg capsules) to …"

2. In the **CLINICAL PHARMACOLOGY** section, Pharmacokinetics subsection, add the following sentence at the end of the 5th paragraph.

   "Azithromycin 250 mg capsules are no longer commercially available. Azithromycin 250 mg tablets are bioequivalent to 250 mg capsules in the fasting state."

3. In the **CLINICAL PHARMACOLOGY** section, Distribution subsection, 2nd paragraph, replace the word "levels" with the word "concentrations" to read:

   "Tissue concentrations have not been …"

4. In the **CLINICAL PHARMACOLOGY** section, Distribution subsection, add the following paragraph at the end of the subsection:

   "Following a regimen of 500 mg on the first day followed by 250 mg daily for 4 days, concentrations in the cerebrospinal fluid were less than 0.01 µg/mL in the presence of non-inflamed meninges."

5. In the **CLINICAL PHARMACOLOGY** section, **Microbiology** subsection, add the following sentence after the listing of "**Other microorganisms"**

   "Beta-lactamase production should have no effect on azithromycin activity."

6. In the **PRECAUTIONS** section, **Information for patients** subsection, delete the 1st paragraph that reads**:**

   "Patients should be cautioned not to take aluminum and magnesium containing antacids and azithromycin by the oral route simultaneously."

7. In the **PRECAUTIONS** section, **Drug Interactions** subsection, add a 3rd paragraph that reads:

   "Drug interaction studies were performed with azithromycin and other drugs likely to be co-administered. (See **CLINICAL PHARMACOLOGY-Drug-Drug Interactions.)** When used in therapeutic doses, azithromycin had a modest effect on the pharmacokinetics of atorvastatin, carbamazepine, cetirizine, didanosine, efavirenz, fluconazole, indinavir, midazolam, rifabutin, sildenafil, theophylline (intravenous and oral), triazolam, trimethoprim/sulfamethoxazole or zidovudine. Co-administration with efavirenz or fluconazole had a modest effect on the pharmacokinetics of azithromycin. No dosage adjustment of either drug is recommended when azithromycin is coadministered with any of these agents.

8. In the **PRECAUTIONS** section, **Drug Interactions** subsection, the last statement should read:

   "Terfenadine, cyclosporine, hexobarbital and phenytoin – elevated concentrations."

The final printed labeling (FPL) must be identical to the package insert submitted on October 11, 2002, and include the revisions listed above.

Please submit the FPL electronically according to the guidance for industry titled Providing Regulatory Submissions in Electronic Format – NDA. Alternatively, you may submit 20 paper 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 supplement NDA 50-733/S-007." Approval of this submission by FDA is not required before the labeling is used.

If you issue a letter communicating important information about this drug product (i.e., a "Dear Health Care Professional" letter), we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH, HFD-410
FDA
5600 Fishers Lane
Rockville, MD 20857

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, call Judit Milstein, Regulatory Project Manager, at (301) 827-2207.

Sincerely,

{See appended electronic signature page}

Janice M. Soreth, MD
Director
Division of Anti-Infective Drug Products
Office of Drug Evaluation IV
Center for Drug Evaluation and Research

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Janice Soreth

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