DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-266/S-002
NDA 21-267/S-003

Pfizer, Inc.
Attention: Elina Srulevitch-Chin
Director
Worldwide Regulatory Strategy
235 East 42nd St.
New York, NY 10017

Dear Ms. Srulevitch-Chin:

Please refer to your supplemental new drug applications, dated February 3, 2003, received February 4, 2003, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act:

NDA #	Drug Product	Supplement number
21-266	VFEND® (voriconazole) Tablets, 50 mg, 200 mg	S-002
21-267	VFEND® (voriconazole) Powder for Injection, 200 mg vial	S-003

These "Changes Being Effected (CBE)" supplemental new drug applications provide for the following revisions to the package insert (additions are double underlined and deletions are ~~struck out~~):

1. **PRECAUTIONS**

• **General** subsection**:**

Some azoles, including voriconazole, have been associated with prolongation of the QT interval on the electrocardiogram. During clinical development and post-marketing surveillance, there have been rare cases of torsade de pointes in patients taking voriconazole. These reports involved seriously ill patients with multiple confounding risk factors, such as history of cardiotoxic chemotherapy, cardiomyopathy, hypokalemia and concomitant medications that may have been contributory.

Voriconazole should be administered with caution to patients with these potentially proarryhthmic conditions.

Rigorous attempts to correct potassium, magnesium and calcium should be made before starting voriconazole.

• **Laboratory Tests** subsection**:**

Electrolyte disturbances such as hypokalemia, hypomagnesemia and hypocalcemia should be corrected prior to initiation of VFEND therapy.

2. **ADVERSE REACTIONS**

•**Less Common Adverse Events** subsection:

Cardiovascular: atrial arrhythmia, atrial fibrillation, AV block complete, bigeminy, bradycardia, bundle branch block, cardiomegaly, cardiomyopathy, cerebral hemorrhage, cerebral ischemia, cerebrovascular accident, congestive heart failure, deep thrombophlebitis, endocarditis, extrasystoles, heart arrest, myocardial infarction, nodal arrhythmia, palpitation, phlebitis, postural hypotension, pulmonary embolus, QT interval prolonged, supraventricular tachycardia, syncope, thrombophlebitis, vasodilatation, ventricular arrhythmia, ventricular fibrillation, ventricular tachycardia (including ~~possible~~ *torsade de pointes)*

3. **DOSAGE AND ADMINISTRATION**

•The following sentence was added before "Use in Adults":

Electrolyte disturbances such as hypokalemia, hypomagnesemia and hypocalcemia should be corrected prior to initiation of VFEND therapy (see PRECAUTIONS).

•The following statements were revised towards the end of this section:

Infusions of blood products ~~and any electrolyte supplementation~~ must not occur simultaneously with VFEND I.V.

Infusions of total parenteral nutrition can occur simultaneously with VFEND I.V.

We have completed the review of these supplemental new drug applications and have concluded that adequate information has been presented to demonstrate that the drug products are safe and effective for use as recommended for use in the agreed upon labeling text and with the minor editorial revision noted below. Accordingly, these supplemental new drug applications are approved effective on the date of this letter.

Please delete the word "approved" in the following sentence in the **REFERENCES** section:

Proposed ~~Approved~~ Standard M38-P. National Committee for Clinical Laboratory Standards, Villanova, Pa.

The final printed labeling (FPL) must be identical to the submitted draft labeling (package insert submitted February 3, 2003) and include the minor editorial revision indicated.

Please submit the copies of final printed labeling (FPL) electronically to each application 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, these submissions should be designated "FPL for approved supplements NDA 21-266/S-002, NDA 21-267/S-003." Approval of these submissions by FDA is not required before the labeling is used.

If a letter communicating important information about these drug products (i.e., a "Dear Health Care Practitioner" letter) is issued to physicians and others responsible for patient care, we request that you submit a copy of the letter to these NDAs and a copy to the following address:

MEDWATCH, HF-2
FDA
5600 Fishers Lane
Rockville, MD 20857

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, please call Robin Anderson, Labeling Reviewer at (301) 827-2127.

Sincerely,

{See appended electronic signature page}

Renata Albrecht, M.D.
Director
Division of Special Pathogen and
Immunologic 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/

Renata Albrecht

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