



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-227/S-011, S-014

Merck & Co., Inc.
Attention: Tamra L. Goodrow, Ph.D.
Director, Regulatory Affairs
BLA-20
P.O. Box 4
West Point, PA 19486-0004

Dear Dr. Goodrow:

Please refer to your supplemental new drug application (S-011) dated June 5, 2003, received June 6, 2003, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for CandesolTM (caspofungin acetate) Injection, 50 mg/vial, 70 mg/vial.

We acknowledge receipt of your submissions dated December 8, 2003 and March 2, 2004.

Your submission of January 29, 2004 constitutes a complete response to our December 4, 2003 letter.

This supplemental new drug application provides for the following revision to the package insert (additions are double underlined and deletions are ~~strikethrough~~):

MICROBIOLOGY

- The *Drug Resistance* subsection was revised to read:

Drug Resistance

~~A study in mice infected with *C. albicans* and treated with orally administered doses of caspofungin suggests that there is a potential for resistance development to occur. *In vitro* resistance development to caspofungin by *Aspergillus* species has not been studied. In limited clinical experience, drug resistance in patients with invasive aspergillosis has not been observed. The incidence of drug resistance by various clinical isolates of *Candida* and *Aspergillus* species is unknown.~~

Drug Resistance

Mutants of *Candida* with reduced susceptibility to caspofungin have been identified in some patients during treatment. Similar observations were made in a study in mice infected with *C. albicans* and treated with orally administered doses of caspofungin. MIC values for caspofungin should not be used to predict clinical outcome, since a correlation

between MIC values and clinical outcome has not been established. The incidence of drug resistance by various clinical isolates of *Candida* and *Aspergillus* species is unknown.

Please refer also to your supplemental new drug application (S-014) dated February 11, 2004, received February 12, 2004, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for CancidasTM (capsfungin acetate) for Injection, 50 mg/vial, 70 mg/vial.

This supplemental new drug application provides for the following revision to the package insert (additions are double underlined and deletions are ~~strikethrough~~):

ADVERSE REACTIONS

- The *General* subsection was revised to read:

General

Possible histamine-mediated symptoms have been reported including ~~isolated~~ reports of rash, facial swelling, pruritus, sensation of warmth, or bronchospasm. Anaphylaxis has been reported during administration of CANCIDAS.

We have completed the review of these supplemental 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 final printed label submitted on March 2, 2004 (enclosed). Accordingly, these supplemental applications are approved effective on the date of this letter.

If a letter communicating important information about this drug product (i.e., a "Dear Health Care Professional" letter) is issued to physicians and others responsible for patient care, we request that you submit a copy of the letter to this NDA 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, call Robin Anderson, R.N., M.B.A., 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
3/17/04 10:45:51 PM