DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 21-227/S-027 **SUPPLEMENT APPROVAL**

Merck Research Laboratories
Attention: Chitrananda Abeygunawardana, Ph.D.
Associate Director, Regulatory Affairs
PO Box 1000
UG2D-068
North Wales PA 19454

Dear Dr. Abeygunawardana:

Please refer to your supplemental new drug application (sNDA) dated and received January 6, 2010, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Cancidas™ (caspofungin acetate) for Injection, 50mg/vial and 70 mg/vial.

This "Changes Being Effected" supplemental new drug application, submitted in response to the Supplement Request Letter issued by the Division on November 30, 2009, provides for the following revisions to the contents of labeling (additions are reflected by underlined text)

1. The **5 WARNINGS AND PRECAUTIONS, 5.2 Hepatic effects** section is revised as follows:

   5.2 Hepatic effects:
   Laboratory abnormalities in liver function tests have been seen in healthy volunteers and in adult and pediatric patients treated with CANCIDAS. In some adult and pediatric patients with serious underlying conditions who were receiving multiple concomitant medications with CANCIDAS, isolated cases of clinically significant hepatic dysfunction, hepatitis, and hepatic failure have been reported; a causal relationship to CANCIDAS has not been established. Patients who develop abnormal liver function tests during CANCIDAS therapy should be monitored for evidence of worsening hepatic function and evaluated for risk/benefit of continuing CANCIDAS therapy.

2. The **8 USE IN SPECIFIC POPULATION**, **8.4 Pediatric Use** section is revised as follows**:**

8.4 Pediatric Use
In clinical trials, 171 pediatric patients (0 months to 17 years of age), including 18 patients who were less than 3 months of age, were given intravenous CANCIDAS. Pharmacokinetic studies enrolled a total of 66 pediatric patients, and an additional 105 pediatric patients received CANCIDAS in safety and efficacy studies [see Clinical Pharmacology (12.3) and Clinical Studies (14.5)]. The majority of the pediatric patients received CANCIDAS at a once-daily maintenance dose of 50 mg/m2 for a mean duration of 12 days (median 9, range 1-87 days). In all studies, safety was assessed by the investigator throughout study therapy and for 14 days following cessation of study therapy. The most common adverse reactions in pediatric patients treated with CANCIDAS were pyrexia (29%), blood potassium decreased (15%), diarrhea (14%), increased aspartate aminotransferase (12%), rash (12%), increased alanine aminotransferase (11%), hypotension (11%), and chills (11%). [see Adverse Reactions (6.2)].
Postmarketing hepatobiliary adverse events have been reported in pediatric patients with serious underlying medical conditions [see Warnings and Precautions 5.2]

We have completed our review of this application. It is approved, effective on the date of this letter, for use as recommended in the enclosed, agreed upon labeling text, which is identical to the content of labeling [21 CFR 314.50(l)(1)(i)] in structured product labeling (SPL) format submitted on January 6, 2010.

We also note that you have updated the **HIGLIGHTS OF PRESCRIBING INFORMATION, RECENT MAJOR CHANGES** section to reflect changes that occurred within the last year.

CONTENT OF LABELING

Please resubmit the enclosed content of labeling in SPL format as soon as possible, but no later than 14 days from the date of this letter. For administrative purposes, please designate this submission, "**SPL for approved NDA 21-227/S-027**."

LETTERS TO HEALTH CARE PROFESSIONALS

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

MedWatch
Food and Drug Administration
5600 Fishers Lane, Room 12B05
Rockville, MD 20857

REPORTING REQUIREMENTS

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, Chief Project Management Staff at (301) 796-0763.

Sincerely,

{See appended electronic signature page}

Ozlem Belen, MD, MPH
Deputy Director for Safety
Division of Special Pathogen and Transplant Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research

Enclosure: Content of Labeling

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-21227	SUPPL-27	MERCK AND CO INC	CANCIDAS (CASPOFUNGIN ACETATE) INJ

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

/s/

OZLEM A BELEN
01/28/2010