DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-227/S-005

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 dated December 11, 2001, received December 12, 2001, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Cancidas™ (capsofungin acetate) for Injection, 50 mg/vial, 70 mg/vial.

We acknowledge receipt of your submissions dated May 15, 2002, June 24, 2002 and October 29, 2002.

This supplemental new drug application provides for the following changes to the Cancidas™ package insert. Added text is noted by double underline and deleted text is noted by ~~strikethrough~~:

1. DOSAGE AND ADMINISTRATION

The *Preparation of Cancidas for use* subsection was revised as follows:

> Do not mix or co-infuse CANCIDAS with other medications, as there are no data available on the compatibility of CANCIDAS with other intravenous substances, additives, or medications. DO NOT USE DILUENTS CONTAINING DEXTROSE (α-D-GLUCOSE), as CANCIDAS is not stable in diluents containing dextrose.
>
> *Preparation of the 70-mg Day 1 loading-dose infusion for Invasive Aspergillosis*
>
> 1. Equilibrate the refrigerated vial of CANCIDAS to room temperature.
> 2. Aseptically add 10.5 mL of 0.9% Sodium Chloride Injection, Sterile Water for Injection, Bacteriostatic Water for Injection with methylparaben and propylparaben, or Bacteriostatic Water for Injection with 0.9% benzyl alcohol to the vial.[a] This reconstituted solution may be stored for up to one hour at ≤25°C (≤77°F).[b]
> 3. Aseptically transfer 10 mL[c] of reconstituted CANCIDAS to an IV bag (or bottle) containing 250 mL 0.9%, 0.45%, or 0.225% Sodium Chloride Injection, or Lactated Ringer's Injection. This infusion solution must be used within 24 hours if stored at ≤25°C

(≤77°F) or within 48 hours if stored refrigerated at 2 to 8°C (36 to 46°F). (If a 70-mg vial is unavailable, see below: *Alternative Infusion Preparation Methods, Preparation of 70-mg Day 1 loading dose from two 50-mg vials.*)

Preparation of the daily 50-mg infusion

1. Equilibrate the refrigerated vial of CANCIDAS to room temperature.
2. Aseptically add 10.5 mL of 0.9% Sodium Chloride Injection, Sterile Water for Injection, Bacteriostatic Water for Injection with methylparaben and propylparaben, or Bacteriostatic Water for Injection with 0.9% benzyl alcohol to the vial.[a] This reconstituted solution may be stored for up to one hour at ≤25°C (≤77°F).[b]
3. Aseptically transfer 10 mL[c] of reconstituted CANCIDAS to an IV bag (or bottle) containing 250 mL 0.9%, 0.45%, or 0.225% Sodium Chloride Injection, or Lactated Ringer's Injection. This infusion solution must be used within 24 hours if stored at ≤25°C (≤77°F) or within 48 hours if stored refrigerated at 2 to 8°C (36 to 46°F). (If a reduced infusion volume is medically necessary, see below: *Alternative Infusion Preparation Methods, Preparation of 50-mg daily doses at reduced volume.*)

Alternative Infusion Preparation Methods

Preparation of 70-mg Day 1 loading dose from two 50-mg vials for Invasive Aspergillosis

Reconstitute two 50-mg vials with 10.5 mL of diluent each (see *Preparation of the daily 50-mg infusion*). Aseptically transfer a total of 14 mL of the reconstituted CANCIDAS from the two vials to 250 mL of 0.9%, 0.45%, or 0.225% Sodium Chloride Injection, or Lactated Ringer's Injection.

Preparation of 50-mg daily doses at reduced volume

When medically necessary, the 50-mg daily doses can be prepared by adding 10 mL of reconstituted CANCIDAS to 100 mL of 0.9%, 0.45%, or 0.225% Sodium Chloride Injection, or Lactated Ringer's Injection (see *Preparation of the daily 50-mg infusion*).

Preparation of a 35-mg daily dose for patients with moderate Hepatic Insufficiency

Reconstitute one 50-mg vial (see above: *Preparation of the daily 50-mg infusion*). Aseptically transfer 7 mL of the reconstituted CANCIDAS from the vial to 250 mL ~~of 0.9% Sodium Chloride Injection~~ or, if medically necessary, to 100 mL of 0.9%, 0.45%, or 0.225% Sodium Chloride Injection or Lactated Ringer's Injection.

Preparation notes:

a The white to off-white cake will dissolve completely. Mix gently until a clear solution is obtained.

b Visually inspect the reconstituted solution for particulate matter or discoloration during reconstitution and prior to infusion. Do not use if the solution is cloudy or has precipitated.

c CANCIDAS is formulated to provide the full labeled vial dose (70 mg or 50 mg) when 10 mL is withdrawn from the vial.

~~d This infusion solution must be used within 24 hours, during which time it should be kept at ≤25°C (≤77°F).~~

2. **HOW SUPPLIED**
The last sentence in this section was revised to read:

> The final patient infusion solution in the IV bag or bottle can be stored at ≤25°C (≤77°F) for 24 hours or at 2 to 8°C (36 to 46°F) for 48 hours.

We have completed the review of this supplemental application, 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 labeling text. Accordingly, this supplemental application is approved effective on the date of this letter.

The final printed labeling (FPL) must be identical to the enclosed draft labeling (text for the package insert submitted October 29, 2002).

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 supplement NDA 21-227/S-005". Approval of this submission by FDA is not required before the labeling is used.

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, 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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