DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 021632/S-013

**SUPPLEMENT APPROVAL**

Vicuron Holdings LLC, a subsidiary of Pfizer, Inc.
Attention: Anne Palestroni
Director, Worldwide Regulatory Strategy
235 East 42nd Street
New York, NY 10017

Dear Ms. Palestroni:

Please refer to your Supplemental New Drug Application (sNDA) dated and received May 12, 2010, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for ERAXIS (anidulafungin) for Injection, 50 mg and 100 mg.

We acknowledge receipt of your amendment dated October 15, 2010.

This "Changes Being Effected" supplemental new drug application proposes the following revisions to the package insert: (~~strikethrough~~ = deleted information and underline = added information)

1. The **MICROBIOLOGY/Drug Resistance** subsection is revised as follows:

   **Drug Resistance**
   ~~Emergence of resistance to anidulafungin has not been studied.~~

   ~~Anidulafungin was active against *Candida albicans* resistant to fluconazole. Cross resistance with other echinocandins has not been studied.~~

   There have been reports of *Candida* isolates with reduced susceptibility to anidulafungin, suggesting a potential for development of drug resistance. The clinical significance of this observation is unknown.

2. In the **PRECAUTIONS/Hepatic Effects** subsection, 3rd sentence, the word "worsening" is deleted as follows:

   **Hepatic Effects**
   Laboratory abnormalities in liver function tests have been seen in healthy volunteers and patients treated with ERAXIS. In some patients with serious underlying medical conditions who were receiving multiple concomitant medications along with ERAXIS, clinically significant hepatic abnormalities have occurred. Isolated cases of significant

hepatic dysfunction, hepatitis, or ~~worsening~~ hepatic failure have been reported in patients; a causal relationship to ERAXIS has not been established. Patients who develop abnormal liver function tests during ERAXIS therapy should be monitored for evidence of worsening hepatic function and evaluated for risk/benefit of continuing ERAXIS therapy.

3. In the **ADVERSE REACTIONS/General** subsection, 1st sentence, the word "bronchospasm" is added as follows:

**General**
Possible histamine-mediated symptoms have been reported with ERAXIS, including rash, urticaria, flushing, pruritus, bronchospasm, dyspnea, and hypotension. These events are infrequent when the rate of ERAXIS infusion does not exceed 1.1 mg/minute.

4. In the **DOSAGE AND ADMINISTRATION/ Preparation of ERAXIS for Administration** subsection, the phrase "in a refrigerator" is added in several sections, and the phrase "**or 84 mL/hr**" is added in the bolded sentence below Table 10:

**Preparation of ERAXIS for Administration**
ERAXIS for Injection must be reconstituted with sterile Water for Injection and subsequently diluted only with ~~only~~ 5% Dextrose Injection, USP or 0.9% Sodium Chloride Injection, USP (normal saline). The compatibility of reconstituted ERAXIS with intravenous substances, additives, or medications other than 5% Dextrose Injection, USP or 0.9% Sodium Chloride Injection, USP (normal saline) has not been established.

*Reconstitution 50 mg/vial*
Aseptically reconstitute each 50 mg vial with 15 mL of sterile Water for Injection to provide a concentration of 3.33 mg/mL. The reconstituted solution can be stored in a refrigerator for up to one hour at 2°C – 8°C (36°F – 46°F) prior to dilution into the infusion solution. Do not freeze.

*Reconstitution 100 mg/vial*
Aseptically reconstitute each 100 mg vial with 30 mL of sterile Water for Injection to provide a concentration of 3.33 mg/mL. The reconstituted solution can be stored in a refrigerator for up to one hour at 2°C – 8°C (36°F – 46°F) prior to dilution into the infusion solution. Do not freeze.

*Dilution and Infusion*
Aseptically transfer the contents of the reconstituted vial(s) into the appropriately sized IV bag (or bottle) containing either 5% Dextrose Injection, USP or 0.9% Sodium Chloride Injection, USP (normal saline). See Table 10 for the dilution and infusion instructions for each dose.

**The rate of infusion should not exceed 1.1 mg/minute (equivalent to 1.4 mL/minute or 84 ml/hour when reconstituted and diluted per instructions).**

If the infusion solution is not used immediately, it should be stored in a refrigerator at 2°C – 8°C (36°F – 46°F). Do not freeze. The infusion solution should be administered within 24 hours of preparation.

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. If particulate matter or discoloration is identified, discard the solution.

5. In the **DOSAGE AND ADMINISTRATION/ Preparation of ERAXIS for Administration/***Dilution and Infusion* subsections, a title is added to Table 10 to read:

**Table 10. Dilution Requirements For ERAXIS Administration**

6. In the **STORAGE** section, the phrase "in a refrigerator" is added as follows:

**Unreconstituted vials**
ERAXIS unreconstituted vials should be stored in a refrigerator at 2°C – 8°C (36°F – 46°F). Do not freeze.

**Reconstituted solution**
ERAXIS reconstituted solution can be stored in a refrigerator at 2°C – 8°C (36°F – 46°F) for up to one hour. Do not freeze.

Chemical and physical in-use stability of the reconstituted solution has been demonstrated for 1 hour at 5ºC (41ºF). .

**Infusion solution**
ERAXIS infusion solution can be stored in a refrigerator at 2°C – 8°C (36°F – 46°F ), but should be administered within 24 hours. Do not freeze.

We also note that your submission contains numerous editorial revisions that do not require our approval.

We have completed our review of this supplemental application, as amended. It is approved, effective on the date of this letter, for use as recommended in the enclosed, agreed-upon labeling text.

## CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, submit, using the FDA automated drug registration and listing system (eLIST), the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format, as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm, that is identical to the enclosed labeling (text for the package insert) and include the labeling changes proposed in any pending "Changes Being Effected" (CBE) supplements. Information on

submitting SPL files using eLIST may be found in the guidance for industry titled "SPL Standard for Content of Labeling Technical Qs and As" at http://www.fda.gov/downloads/DrugsGuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf.

The SPL will be accessible from publicly available labeling repositories.

Also within 14 days, amend all pending supplemental applications for this NDA, including pending "Changes Being Effected" (CBE) supplements, for which FDA has not yet issued an action letter, with the content of labeling [21 CFR 314.50(l)(1)(i)] in MS Word format that includes the changes approved in this supplemental application.

**PROMOTIONAL MATERIALS**

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit the following, in triplicate, (1) a cover letter requesting advisory comments, (2) the proposed materials in draft or mock-up form with annotated references, and (3) the package insert(s) to:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Drug Marketing, Advertising, and Communications
5901-B Ammendale Road
Beltsville, MD 20705-1266

You must submit final promotional materials and package insert(s), accompanied by a Form FDA 2253, at the time of initial dissemination or publication [21 CFR 314.(b)(3)(i)]. Form FDA 2253 is available at http://www.fda.gov/opacom/morechoices/fdaforms/cder.html; instructions are provided on page 2 of the form. For more information about submission of promotional materials to the Division of Drug Marketing, Advertising, and Communications (DDMAC), see http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm.

**LETTERS TO HEALTH CARE PROFESSIONALS**

If you decide to 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, at least 24 hours prior to issuing the letter, an electronic copy of the letter to this NDA to the following address:

MedWatch Program
Office of Special Health Issues
Food and Drug Administration
10903 New Hampshire Ave
Building 32, Mail Stop 5353
Silver Spring, MD 20993

**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 Mr. Gregory DiBernardo, Regulatory Project Manager, at (301) 796-1600.

Sincerely,

*{See appended electronic signature page}*

Ozlem Belen, M.D., M.P.H.
Deputy Director for Safety
Division of Special Pathogen and Transplant Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research

ENCLOSURE: Package Insert

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

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/s/

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OZLEM A BELEN
11/04/2010