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## New Antifungal Drug: ERAXIS™ (anidulafungin)

The following is a brief summary of a newly approved drug. The complete prescribing information should be consulted before use in a specific patient.

Serious fungal infections often affect patients with compromised immune systems. Eraxis (anidulafungin) is a new antifungal drug that is administered by intravenous infusion. It was recently approved by the FDA for treating candidemia, esophageal candidiasis, and other forms of *Candida* infections (intra-abdominal abscess, peritonitis). Eraxis has not been studied in endocarditis, osteomyelitis, and meningitis due to *Candida*, and has not been studied in sufficient numbers of neutropenic patients to determine efficacy in this group. Eraxis has been studied in combination with liposomal amphotericin B in treating invasive aspergillosis; clinical studies are ongoing.

**Pharmacology & Mechanism of Action:** Eraxis is in the echinocandin pharmacological class, as are Cancidas (caspofungin) and Mycamine (micafungin). This antifungal group is attractive because of a lack of nephrotoxicity and few drug interactions. These drugs have fungicidal activity rather than a fungistatic mechanism of action. Anidulafungin inhibits glucan synthase, an enzyme required to form the fungal cell wall. This enzyme is not present in mammalian cells, which should result in fewer adverse drug effects. Anidulafungin is active against *Candida albicans*, *C. glabrata*, *C. parapsilosis*, and *C. tropicalis*. It is effective against fluconazole-resistant strains. Anidulafungin may be more active against *Aspergillus* sp. than caspofungin based on MIC data in some studies.

**Contraindications, Warnings, & Precautions:** Eraxis is contraindicated in patients with known hypersensitivity to anidulafungin or any of its components. Some healthy volunteers and patients receiving Eraxis have developed clinically significant hepatic abnormalities. Eraxis has not been sufficiently studied in pediatric patients to completely establish safety and efficacy in that group, although a small clinical study of pediatric patients was done.

**Drug Interactions:** Unlike caspofungin, no dosage adjustment is needed for cyclosporine when it is used with anidulafungin. Cyclosporin can increase the steady-state levels of anidulafungin by 22%, but no dosage adjustment is warranted according to the manufacturer. No dosage adjustment is needed for either agent with concomitant use of voriconazole, tacrolimus, AmBisome or rifampin. Eraxis is not expected to have any interaction with drugs metabolized by cytochrome P450 isoenzymes. No clinically relevant drug-drug interactions are known at this time.

**Dosing:** Dose adjustments are not required for gender, geriatric patients, race, or HIV status. The dose is not adjusted for patients with mild, moderate or severe hepatic insufficiency, or for patients with any degree of renal insufficiency including those on hemodialysis. Anidulafungin is not metabolized in the liver. It is not dialyzable and may be given without regard to the timing of hemodialysis.

- **Candidemia and other *Candida* infections (intra-abdominal abscess, peritonitis):** 200 mg single loading dose followed by a 100 mg daily dose thereafter. Duration of treatment is based on clinical response; in general, therapy should continue for at least 14 days after the last positive culture
- **Esophageal candidiasis:** 100 mg single loading dose followed by a 50 mg daily dose thereafter. Patients should be treated for a minimum of 14 days, and for at least 7 days following resolution of symptoms. Duration of treatment is based on clinical response. Because of the risk of relapse of esophageal candidiasis in patients with HIV infections, suppressive antifungal therapy may be considered after a course of treatment.



**Adverse Reactions:** Possible histamine-mediated symptoms have been reported, including rash, urticaria, flushing, pruritus, dyspnea, and hypotension. These events appear to be infrequent when the rate of infusion does not exceed 1.1 mg/minute in adults. Other treatment-related adverse drug reactions included diarrhea, elevated hepatic enzymes, hypokalemia, deep vein thrombosis, neutropenia, leukopenia, nausea/vomiting, pyrexia, headache, rash (unspecified) and phlebitis.

**Monitoring:** Liver function tests. Patients who develop abnormal liver function tests should be monitored for evidence of worsening hepatic function and evaluated for risk/benefit of continuing Eraxis therapy.

**Preparation, Stability and Storage:** Eraxis requires a special diluent (20% w/w Dehydrated Alcohol in Water for Injection), which is provided with the drug. Each 50mg vial requires 15 mL of this special diluent. Once the lyophilized product is reconstituted, it should be further diluted and administered within 24 hours. The drug solution must be diluted with only 5% Dextrose or 0.9% Sodium Chloride (normal saline) and stored at room temperature prior to administration. Do not freeze the drug powder or the infusion solution. The concentration of the final solution for administration should be 0.5 mg/mL. Eraxis should not be mixed with any other medications.

**Administration:** The rate of infusion should not exceed 1.1 mg/minute and should be completed within 24 hours of preparing the drug solution.

References:

1. Manufacturer's information and
2. Clinical Pharmacology [database online], Tampa FL: Gold Standard, Inc.; 2006. URL: <http://cp.gsm.com>. Updated 3/16/06.

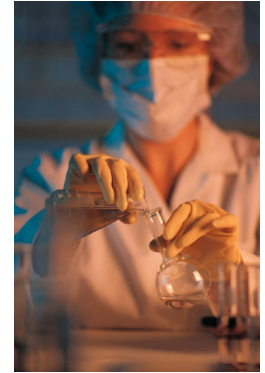
## Use of Vfend for Invasive Aspergillosis

The Infectious Diseases Society of America (IDSA) publishes treatment guidelines for many infectious diseases. One of the IDSA committees has recently proposed changes to the practice guidelines for invasive aspergillosis, a highly lethal fungal infection that occurs most commonly in the immunocompromised patient.

The current IDSA "Practice Guidelines for Diseases Caused by *Aspergillus*" were published in 2000. Those guidelines include prompt and aggressive work-up of invasive aspergillosis, and emphasize the need for initiating antifungal therapy based upon suspicion of the diagnosis, which may be before definite proof is available. Intravenous therapy should be used initially in rapidly progressing disease. The Practice Guidelines discuss amphotericin B deoxycholate (conventional amphotericin) as the drug most often used for this infection, and present guidelines for dosing. Lipid formulations of amphotericin are recommended for patients with impaired renal function or for those who develop nephrotoxicity while receiving conventional amphotericin. Oral itraconazole is listed as an alternative for some patients, if they respond to initial intravenous therapy.

Now, new clinical evidence may support a change in initial treatment of invasive aspergillosis. In a recent clinical trial of patients with invasive aspergillosis, about 53% of patients treated with Vfend (voriconazole) achieved a complete or partial response, compared with about 32% of patients treated with amphotericin B. Vfend also has the advantage of being available in an oral form, unlike amphotericin. Further clinical trials are being planned to test whether combination therapy improves outcomes in cases where Vfend does not cure.

The IDSA has not yet finalized any proposed changes to the guidelines, which were presented orally and in abstract form at the IDSA conference in October, 2005. However, it is worth noting that Vfend may be an option for initial treatment of invasive aspergillosis, and clinicians should watch for further published guidelines from the IDSA.



*Liver function tests are an important part of monitoring Eraxis therapy*

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*Aspergillus*