

Errata Sheet For The Background Document for the January 10, 2001
Antiviral Drug Products Advisory Committee Meeting

1. Under **Pharmacokinetics** on top of page 6, the sentence
"In vitro incubation experiments suggest that 2 potentially reactive intermediates (M1 and M2) are formed during the degradation of caspofungin to L-747969, and that these form covalent adducts to protein"

should read

"In vitro incubation experiments suggest that 2 potentially reactive intermediates are formed during the degradation of caspofungin to L-747969, and that these form covalent adducts to protein."
2. Under **Pharmacokinetics; Drug Drug Interactions** in the middle of page 9, the sentence
"Although cyclosporine C24 changed 2 fold, the increase in AUC 0-24 was approximately 35%"

should read

"Although caspofungin C24 changed 2 fold, the increase in AUC 0-24 was approximately 35%."
3. Under **III. Efficacy, 1. Data Source** on page 11, the sentence
"Fifty-five percent of 87 patients with pulmonary aspergillosis and 61% of 42 patients with disseminated aspergillosis were identified by autopsy cultures in the historical control study."

should read

"Fifty-five percent of 87 patients with pulmonary aspergillosis and 61% of 42 patients with disseminated aspergillosis had evidence of aspergillosis based on autopsy in the historical control study, though only a total of 17 patients met diagnostic criteria based on autopsy cultures in the historical control study."
4. Under **III. Efficacy, 1. Data Source** on page 11, the sentence
"On the other hand, 12 (17%) patients in the prospective open label study were considered for inclusion without a positive culture if an investigational test (galactomannan ELISA or PCR) were positive."

should read

"On the other hand, 8/69 (8.6%) patients in the prospective open label study were considered for inclusion without a positive culture or histopathology if an investigational test (galactomannan ELISA or PCR) were positive."
5. Under **Applicant efficacy analysis of CANCIDAS as salvage therapy in invasive aspergillosis refractory to or intolerant of standard antifungal therapy**, middle of page 13, the sentence
"A greater proportion of patients in the historical control study had definite infections and more disseminated infections"

should read

"A similar proportion of patients in the historical control study had definite infections and/or disseminated infections."

6. Under **Efficacy of CANCIDAS in patients with invasive aspergillosis involving the central nervous system** page 17, the sentence

"Nevertheless, in Study 019, six patients were considered to have possible CNS aspergillosis on entry into the study.... The first was a 66 year old diabetic female (#366) diagnosed with Aspergillus versicolor skull osteomyelitis following a penetrating skull injury."

should read

"Nevertheless, in Study 019, 1 patient was considered to have definite CNS aspergillosis and 5 patients to have possible aspergillosis upon entry into the study. ... The first was a 66 year old diabetic female (#366) diagnosed with definite Aspergillus flavus skull osteomyelitis and brain abscess following a penetrating skull injury." In addition, Table 4 should be amended to state that patient #366 had "definite CNS" as their her diagnosis.

7. Under **Section IV. Safety of CANCIDAS in clinical studies of healthy subjects in the clinical pharmacology studies and in patients in the Invasive Aspergillosis and Candida mucosal infections studies** page 19, the sentence

"Findings in preclinical studies in animals were notable for histamine release-like reactions, eosinophilia, and frequent elevations of transaminases."

should read

"Findings in preclinical studies in animals were notable for histamine release-like reactions and frequent elevations of transaminases."

8. Under **Clinical and Laboratory Safety in the Clinical Pharmacology Studies** page 20, the sentence

"The most frequent laboratory adverse event was an elevation of liver function tests. This appeared to be dose related, occasionally associated with an increase in serum bilirubin, and exacerbated by cyclosporin co-administration."

should read

"The most frequent laboratory adverse event was an elevation of liver function tests. For the subjects given caspofungin plus other drugs, especially cyclosporin A, this may be dose-related."

9. For **Table 3: Clinical Efficacy Rates for Study 019 as per the Expert Panel /FDA Analyses compared to outcomes in the historical Controls (study 028)** page 14, the refractory expert panel cell (Column 2, Row 3) currently reads

"15/44 34.1%"

should read

"19/53 35.8%"