CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

22-027

CLINICAL PHARMACOLOGY AND BIOPHARMACEUTICS REVIEW(S)

CLINICAL PHARMACOLOGY REVIEW

NDA: 22-027	Submission Date(s): 12/22/2005
Drug	Posaconazole
Trade Name	Noxafil
Reviewer	Seong H, Jang, Ph.D.
OCP Team Leader	Philip M. Colangelo, Pharm.D., Ph.D.
OCP Division	DCP 4
OND division	ODE IV DSPTP
Sponsor	Schering-Plough Corp.
Relevant IND(s)	51,662
Submission Type; Code	Original, 1S (NME)
Formulation; Strength(s)	Oral suspension 40 mg/mL (105 mL)
Indication	Treatment of oropharyngeal candidiasis, including infections refractory to itraconazole and fluconazole
Dosage and Administration	Oropharyngeal Candidiasis: Loading dose o' [redacted] nen 100 mg QD for 13 days Refractory Oropharyngeal Candidiasis: 400 mg BID with a meal or with a nutritional supplement in patients who cannot tolerate a full meal

Posaconazole (POS, SCH 56592) is a triazole antifungal agent and, like other azoles such as fluconazole, itraconazole, and voriconazole, blocks ergosterol biosynthesis of yeast and filamentous fungi by inhibiting the enzyme lanosterol 14α-demethylase (CYP51, Erg11p). The drug formulation in this NDA is an oral suspension (40 mg/mL). The proposed indications for NDA 22-027 is treatment of oropharyngeal candidiasis (OPC), including infections refractory to itraconazole and fluconazole. The NDA 22-003, supporting the use of POS for prophylaxis of invasive *Aspergillus* and *Candida* infections in patients, 13 years of age and older, who are at high risk of developing these infections due to being severely immunocompromised, such as hematopoietic stem cell transplant recipients with Graft-versus-host disease or those with hematopoietic amlignacies with prolonged neutropenia from chemotherapy, was approved on September 15, 2006.

The efficacy and safety of POS for treatment of OPC, including infections refractory to itraconazole and fluconazole, were evaluated in two pivotal Phase III studies. There were limited PK data (e.g., one plasma concentration per patient after last dose of POS) in the study reports, which were not appropriate to evaluate potential exposure-response relationships for the treatment of OPC. These POS plasma concentrations are listed in the tables of Attachment 1. Therefore, additional Clinical Pharmacology review is not needed for NDA 22-027.

Seong H. Jang, Ph.D.
Reviewer
Clinical Pharmacology
Pharmacometrics
DCP4/OCPB

Concurrence

Phil Colangelo, Pharm.D., Ph.D.
Team Leader
Clinical Pharmacology
DCP4/OCPB

Attachment 1

Posaconazole plasma concentrations

(Studies C/I97-331 and C/I97-330)

4 Page(s) Withheld

X § 552(b)(4) Trade Secret / Confidential

_____ § 552(b)(4) Draft Labeling

_____ § 552(b)(5) Deliberative Process

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/s/

Seong Jang
10/18/2006 02:13:16 PM
BIOPHARMACEUTICS

Phil Colangelo
10/20/2006 11:18:12 AM
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