

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

205053Orig1s000

STATISTICAL REVIEW(S)

STATISTICS FILING CHECKLIST FOR A NEW NDA/BLA

NDA Number: 205-053

Applicant: Merck

Stamp Date: 1/25/13

Drug Name: Noxafil
(posaconazole) Tablets

NDA/BLA Type: Priority

On **initial** overview of the NDA/BLA application for RTF:

	Content Parameter	Yes	No	NA	Comments
1	Index is sufficient to locate necessary reports, tables, data, etc.	X			
2	ISS, ISE, and complete study reports are available (including original protocols, subsequent amendments, etc.)	X			No ISE since PK bridging
3	Safety and efficacy were investigated for gender, racial, and geriatric subgroups investigated (if applicable).	X			
4	Data sets in EDR are accessible and do they conform to applicable guidances (e.g., existence of define.pdf file for data sets).	X			

IS THE STATISTICAL SECTION OF THE APPLICATION FILEABLE? Yes

If the NDA/BLA is not fileable from the statistical perspective, state the reasons and provide comments to be sent to the Applicant. N/A

Please identify and list any potential review issues to be forwarded to the Applicant for the 74-day letter.

Content Parameter (possible review concerns for 74-day letter)	Yes	No	NA	Comment
Designs utilized are appropriate for the indications requested.	X			
Endpoints and methods of analysis are specified in the protocols/statistical analysis plans.	X			
Interim analyses (if present) were pre-specified in the protocol and appropriate adjustments in significance level made. DSMB meeting minutes and data are available.			X	
Appropriate references for novel statistical methodology (if present) are included.			X	
Safety data organized to permit analyses across clinical trials in the NDA/BLA.	X			
Investigation of effect of dropouts on statistical analyses as described by applicant appears adequate.			X	

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This NDA is for Noxafil (posaconazole) Tablets. Posaconazole is currently approved as an oral suspension for the indications of 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 (HSCT) recipients with graft-versus-host disease (GVHD) or those with hematologic malignancies with prolonged neutropenia from chemotherapy. It is also approved for the treatment of oropharyngeal candidiasis, including oropharyngeal candidiasis refractory to itraconazole and/or fluconazole. In order to increase the absorption of posaconazole oral suspension, it is necessary to take posaconazole oral suspension multiple times per day with a full meal. (b) (4)

The development program for posaconazole tablet for the prophylaxis indication was based on a PK bridging strategy to the posaconazole oral suspension. Five clinical studies in healthy volunteers and one pivotal uncontrolled clinical study in patients were conducted with posaconazole oral tablet. The pivotal clinical study conducted in patients was primarily designed to fully characterize the PK and assess safety of posaconazole tablet in neutropenic subjects (AML and MDS) and subjects who had undergone a HSCT and were under treatment for GVHD. Efficacy was not a primary variable to be assessed in this study and was limited to a descriptive assessment. This study (P05615) was a two part study. In part 1, two sequential and escalating dosing cohorts (200 mg and 300 mg) were evaluated with serial PK sampling to characterize the PK profile. Only neutropenic subjects were enrolled in Part 1. In Part 2, all subjects received the 300 mg dose regimen and the population was expanded to also include subjects who had undergone a HSCT. Sparse PK sampling was performed on all subjects in Part 2. In Part 1, 20 patients received 200 mg and 34 patients received 300 mg. In Part 2, 176 patients received 300 mg.

Since there are no pivotal efficacy studies and the studies conducted are PK studies which are primarily reviewed by Clinical Pharmacology, input in the review of this application by Statistics will be limited to any specific requests made by the Medical Officer.

Cheryl Dixon, Ph.D.	March 1, 2013
Reviewing Statistician	Date
Karen Higgins, Sc.D.	March 1, 2013
Supervisor/Team Leader	Date

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

/s/

CHERYL A DIXON
03/04/2013

KAREN M HIGGINS
03/04/2013