DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 022003/S-018, S-020
NDA 205053/S-002, S-004
NDA 205596/S-001, S-003

SUPPLEMENT APPROVAL

Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc.
Attention: Joanna Pols, PhD
Director, Global Regulatory Affairs
126 E. Lincoln Avenue, P.O. Box 2000
RY34-B188
Rahway, NJ 07065-0900

Dear Dr. Pols:

Please refer to your Supplemental New Drug Applications (sNDAs) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for the following:

Name of Drug Product	NDA #	Supplement #	Submission Date
Noxafil (posaconazole) oral suspension, 40 mg/mL	022003	S-018	August 20, 2015
Noxafil (posaconazole) delayed-release tablets, 100 mg	205053	S-002	August 20, 2015
Noxafil (posaconazole) injection, 18 mg/mL	205596	S-001	May 13, 2015
Noxafil (posaconazole) oral suspension, 40 mg/mL	022003	S-020	October 23, 2015
Noxafil (posaconazole) delayed-release tablets, 100 mg	205053	S-004	October 23, 2015
Noxafil (posaconazole) injection, 18 mg/mL	205596	S-003	October 23, 2015

These "Prior Approval" supplemental new drug applications provide for the following updates to the prescribing information (PI):

May 13, and August 20, 2015 Submissions

- Changes to the **DOSAGE AND ADMINISTRATION** section (2), Important Administration Instructions for Noxafil Injection, Noxafil Delayed-Release Tablets and Noxafil Oral Suspension (2.1) and Dosage, Preparation, Intravenous Line Compatibility and Administration of Noxafil Injection (2.2). Specifically, section 2.2 has been updated to remove the specific size of the intravenous diluent bag (150 mL), and allow dosing of diluted intravenous solution at a concentration range between 1 mg/mL and 2 mg/mL. Additional compatible diluents have been

added and separate tables for compatible diluents and compatible drugs have been created. Minor editorial revisions have been made throughout the PI.

These "Prior Approval" supplemental new drug applications provide for the following updates to the Labeling:

October 23, 2015 Submission

- Updates to the prescribing information (PI) with information concerning the non-interchangeability between Noxafil Delayed-Release Tablets and Noxafil Oral Suspension as requested in the Agency's letter of September 25, 2015. Specifically, the **HIGHLIGHTS, DOSAGE AND ADMINISTRATION** section (2), and the **PATIENT COUNSELING INFORMATION** section (17) of the PI have been updated.

- Editorial revisions to the United States Patient Package Information (USPPI) to provide for consistency with patient labeling practice and updates to the PI.

- Revisions to the Oral Suspension Carton labeling and Delayed-Release Tablet Container label for consistency with the PI.

APPROVAL & LABELING

We have completed our review of these supplemental applications. They are 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 the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format using the FDA automated drug registration and listing system (eLIST), as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm. Content of labeling must be identical to the enclosed labeling (text for the package insert, text for the patient package insert), with the addition of any labeling changes in pending "Changes Being Effected" (CBE) supplements, as well as annual reportable changes not included in the enclosed labeling.

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 that includes labeling changes for these NDAs, including 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 these supplemental applications, as well as annual reportable changes and annotate each change. To facilitate review of your submissions, provide a highlighted or marked-up copy that shows all changes, as

well as a clean Microsoft Word version. The marked-up copy should provide appropriate annotations, including supplement number(s) and annual report date(s).

CARTON AND IMMEDIATE CONTAINER LABELS

Submit final printed carton and immediate container labels that are identical to the enclosed carton and immediate container labels as soon as they are available, but no more than 30 days after they are printed. Please submit these labels electronically according to the guidance for industry *Providing Regulatory Submissions in Electronic Format – Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications (June 2008)*. Alternatively, you may submit 12 paper copies, with 6 of the copies individually mounted on heavy-weight paper or similar material. For administrative purposes, designate these submissions as "**Final Printed Carton and Container Labels for approved NDA 22003/S-018, S-020; Final Printed Carton and Container Labels for approved NDA 205053/S-002, S-004; and Final Printed Carton and Container Labels for approved NDA 205596/S-001, S-003**", respectively. Approval of these submissions by FDA is not required before the labelings are used.

Marketing the product(s) with FPL that is not identical to the approved labeling text may render the products misbranded and unapproved new drugs.

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 Alison Rodgers, Regulatory Project Manager, at (301) 796-0797.

Sincerely,

{See appended electronic signature page}

Joseph Toerner, MD, MPH
Deputy Director for Safety
Division of Anti-Infective Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research

ENCLOSURE(S):
Content of Labeling
Patient Package Information
Carton and Container Labeling

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

/s/

JOSEPH G TOERNER
11/13/2015