DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 205053

NDA APPROVAL

Merck Sharp & Dohme Corp.
Attention: Scott L. Grossman, PhD
Director, Global Regulatory Affairs
351 North Sumneytown Pike
P.O. Box 1000, Mailstop UG2CD48
North Wales, PA 19454-2505

Dear Dr. Grossman:

Please refer to your New Drug Application (NDA) dated January 24, 2013, received January 25, 2013, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Noxafil (posaconazole) delayed-release tablets, 100 mg.

We acknowledge receipt of your amendments dated February 15, March 5, April 29, May 8, 13, and 15, June 12, 13, and 27, July 2, and 26, August 19, and 29, September 10, and 27, October 2, and 10, and November 6, and 25, 2013.

This new drug application provides for the use of Noxafil (posaconazole) delayed-release tablets, 100 mg, for the 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 hematologic malignancies with prolonged neutropenia from chemotherapy.

We have completed our review of this application, as amended. It is approved, effective on the date of this letter, for use as recommended in the enclosed agreed-upon labeling text.

WAIVER OF HIGHLIGHTS SECTION

We are waiving the requirements of 21 CFR 201.57(d)(8) regarding the length of Highlights of prescribing information. This waiver applies to all future supplements containing revised labeling unless we notify you otherwise.

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). Information on submitting SPL files using eLIST may be found in the guidance for industry *SPL Standard for Content of Labeling Technical Qs and As*, available at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf.

The SPL will be accessible via publicly available labeling repositories.

IMMEDIATE CONTAINER LABEL

Submit a final printed immediate container label that is identical to the enclosed label submitted on **October 2, 2013**, as soon as it is available, but no more than 30 days after it is printed. Please submit this label 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 this submission "**Final Printed Container Label for approved NDA 205053**." Approval of this submission by FDA is not required before the labeling is used.

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

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication(s) in pediatric patients unless this requirement is waived, deferred, or inapplicable.

We are waiving the pediatric study requirement for ages 0 to less than two years because the necessary studies are impossible or highly impracticable. This is because hematologic malignancies are not likely to occur in children less than one year and use of antifungal prophylaxis is infrequent in pediatric patients with hematological malignancies under two years of age.

We are deferring submission of your pediatric study for ages two to less than 18 years for this application because this product is ready for approval for use in adults and the pediatric studies have not been completed.

Your deferred pediatric studies required by section 505B(a) of the FDCA are required postmarketing studies. The status of these postmarketing studies must be reported annually according to 21 CFR 314.81 and section 505B(a)(3)(B) of the FDCA. These required studies are listed below.

2090-1: Conduct a trial in patients, ages 2 to < 18 years, to evaluate the pharmacokinetic (PK), safety, and tolerability of two new formulations of posaconazole (IV solution and/or new age-appropriate oral formulation) in immunocompromised pediatric patients with known or expected neutropenia.

Final Protocol Submission: 09/30/14
Trial Completion: 06/30/17
Final Report Submission: 09/30/17

If the trial for PMR 2090-1 fails to find a pediatric dosing regimen that provides pediatric patients with exposures similar to those in adult patients, then the following efficacy trial (PMR 2090-2) will be required, provided a safe and tolerable dosage regimen can still be identified. If the trial for PMR 2090-1 is successful in determining a pediatric dosing regimen, you may request release from PMR 2090-2.

2090-2: Conduct a comparative, double-blind, randomized, multi-center trial, in patients ages 2 to < 18 years, to evaluate the safety, efficacy, and tolerability of posaconazole for the prophylaxis of invasive fungal infections (IFI) in pediatric patients with known or expected neutropenia.

Final Protocol Submission: 09/30/17
Trial Completion: 11/30/20
Final Report Submission: 03/31/21

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit, in triplicate, a cover letter requesting advisory comments, the proposed materials in draft or mock-up form with annotated references, and the package insert to:

Food and Drug Administration
Center for Drug Evaluation and Research
Office of Prescription Drug Promotion
5901-B Ammendale Road
Beltsville, MD 20705-1266

As required under 21 CFR 314.81(b)(3)(i), you must submit final promotional materials, and the package insert, at the time of initial dissemination or publication, accompanied by a Form FDA 2253. For instruction on completing the Form FDA 2253, see page 2 of the Form. For more information about submission of promotional materials to the Office of Prescription Drug Promotion (OPDP), see http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm.

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}

Katherine A. Laessig, MD
Deputy Director
Division of Anti-Infective Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research

Enclosure(s):
Content of Labeling
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/

KATHERINE A LAESSIG
11/25/2013