NDA 50-689/S-016

Pharmacia and Upjohn Company
Attention: Beatrice A. Curran
Associate Director, Worldwide Regulatory Strategy
235 East 42nd Street
New York, NY 10017

Dear Ms. Curran:

Please refer to your supplemental new drug application dated and received November 16, 2007, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Mycobutin®(rifabutin) Capsules, 150 mg.

This "Special Supplement - Changes Being Effected" supplemental new drug application provides for revisions to the package insert for Mycobutin® to ensure consistency in the communication of the risks of *Clostridium difficile* associated disease with the use of antimicrobial products, including rifabutin, as follows (additions are indicated by underlined):

1. In the **WARNINGS** section the following text was added as the forth, fifth, and sixth paragraphs:

   Clostridium difficile associated diarrhea (CDAD) has been reported with use of nearly all antibacterial agents, including MYCOBUTIN (rifabutin capsules, USP), and may range in severity from mild diarrhea to fatal colitis. Treatment with antibacterial agents alters the normal flora of the colon leading to overgrowth of *C. difficile*.

   C. difficile produces toxins A and B which contribute to the development of CDAD. Hypertoxin producing strains of *C. difficile* cause increased morbidity and mortality, as these infections can be refractory to antimicrobial therapy and may require colectomy. CDAD must be considered in all patients who present with diarrhea following antibiotic use. Careful medical history is necessary since CDAD has been reported to occur over two months after the administration of antibacterial agents.

   If CDAD is suspected or confirmed, ongoing antibiotic use not directed against *C. difficile* may need to be discontinued. Appropriate fluid and electrolyte management, protein supplementation, antibiotic treatment of *C. difficile*, and surgical evaluation should be instituted as clinically indicated.

2. In the **PRECAUTIONS/Information for Patients** subsection, The following text was added as the third paragraph:

   Diarrhea is a common problem caused by antibiotics which usually ends when the antibiotic is discontinued. Sometimes after starting treatment with antibiotics, patients can develop watery and bloody stools (with or without stomach cramps and fever) even as late as two or more months after having taken the last dose of the antibiotic. If this occurs, patients should contact their physician as soon as possible.

We completed our review of this application, and it is approved, effective on the date of this letter, for use as recommended in the labeling text submitted November 16, 2007.

If you have any questions, please call Christine Lincoln, RN, M.S., MBA, Regulatory Health Project Manager, at (301) 796-1600.

Sincerely,

{See appended electronic signature page}

Renata Albrecht, M.D.
Director
Division of Special Pathogen and Transplant Products
Office Antimicrobial Products
Center for Drug Evaluation and Research

ENCLOSURE: PPI

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

/s/

Renata Albrecht

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