DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 50-662/S-039
NDA 50-698/S-021
NDA 50-775/S-009

Abbott Laboratories
Attention: Mary Konkowski, Manager
Global Pharmaceutical Regulatory Affairs
Dept. 491, Bldg. AP30-1NE
200 Abbott Park Road
Abbott Park, Illinois 60064-6157

Dear Ms Konkowski:

Please refer to your supplemental new drug applications dated January 5, 2006, received January 6, 2006 submitted under 505(b) of the Federal Food, Drug, and Cosmetic Act for:

NDA 50-662/S-039 Biaxin Filmtab (clarithromycin tablets)
NDA 50-698/S-021 Biaxin Granules (clarithromycin for oral suspension)
NDA 50-775/S-009 Biaxin XL Filmtabs (clarithromycin extended-release tablets)

This application is subject to the exemption provisions contained in section 125(d) (2) of Title I of the FDA Modernization Act of 1997.

These supplemental new drug applications provide for changes to the **PRECAUTIONS -** Drug Interactions section of the labeling.

We completed our review of these applications. These applications are approved, effective on the date of this letter, for use as recommended in the agreed-upon labeling text and with the minor editorial revisions listed below.

The following paragraph should be added under WARNINGS section (second to last paragraph) instead of the **PRECAUTIONS -** General section:

"There have been post-marketing reports of colchicine toxicity with concomitant use of clarithromycin and colchicine, especially in the elderly, some of which occurred in patients with renal insufficiency. Deaths have been reported in some such patients. (See **PRECAUTIONS.**)"

The statement proposed for the Drug Interactions section (the twelfth paragraph) is revised as follows:

"Colchicine is a substrate for both CYP3A and the efflux transporter, P-glycoprotein (Pgp). Clarithromycin and other macrolides are known to inhibit CYP3A and Pgp. When clarithromycin and colchicine are administered together, inhibition of Pgp and/or CYP3A by

clarithromycin may lead to increased exposure to colchicine. Patients should be monitored for clinical symptoms of colchicine toxicity. (See **WARNINGS.**)"

The statement proposed for the Precautions - Geriatric Use section is revised as follows:

"In a steady-state study in which healthy elderly subjects (age 65 to 81 years old) were given 500 mg every 12 hours, the maximum serum concentrations and area under the curves of clarithromycin and 14-OH clarithromycin were increased compared to those achieved in healthy young adults. These changes in pharmacokinetics parallel known age-related decreases in renal function. In clinical trials, elderly patients did not have an increased incidence of adverse events when compared to younger patients. Dosage adjustment should be considered in elderly patients with severe renal impairment. (See **WARNINGS and PRECAUTIONS.**)"

The statement proposed for the **ADVERSE REACTIONS** - Post-Marketing Experience:

"There have been post-marketing reports of colchicine toxicity with concomitant use of clarithromycin and colchicine, especially in the elderly, some of which occurred in patients with renal insufficiency. Deaths have been reported in some such patients. (See **WARNINGS and PRECAUTIONS.**)"

The final printed labeling (FPL) must be identical, and include the minor editorial revisions indicated, to the text for the patient package insert. These revisions are terms of the approval of these applications.

If you issue a letter communicating important information about this drug product (i.e., a "Dear Health Care Professional" letter), we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH
Food and Drug Administration
WO 22, Room 4447
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

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 Carmen DeBellas, Regulatory Project Manager, at (301) 301-796-1203.

Sincerely,

{See appended electronic signature page}

Janice M. Soreth, MD
Director
Division of Anti-Infective and Ophthalmology Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research

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

/s/

Janice Soreth

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