DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville MD 20857

TRANSMITTED VIA FACSIMILE

SEP 18 1998

Ann Karen Henry
Director, Regulatory Affairs, Advertising
Abbott Laboratories
Dept. 491, Bldg. AP6B-1
100 Abbott Park Road
Abbott Park, IL 60064-3500

RE: NDA # 50-662
Biaxin (clarithromycin) Filmtab, Granules
MACMIS ID # 6851

Dear Ms. Henry:

The Division of Drug Marketing, Advertising, and Communications, (DDMAC) as part of its routine monitoring and surveillance program, has reviewed materials that are used to promote Abbott Laboratories' (Abbott) product, Biaxin Filmtab, Granules (Biaxin). These materials included posters #801-010-2346 A,B,C,D,E, 709-023-1559E, leaflet 712-010-2048, Abbott's Internet home page, and lunch box 709-023-1563 submitted under cover of FDA Form 2253. DDMAC finds the dissemination of these posters and lunch box to be in violation of the Federal, Food, Drug, and Cosmetic (the Act) and the applicable regulations.

Specifically, DDMAC objects to the following:

Failure to Provide Fair Balance

Posters #801-010-2346 A,B,C,D,E are lacking in fair balance or otherwise misleading because they fail to disclose any information about the risks associated with the use of Biaxin. Specifically, the posters contain several promotional claims regarding the effectiveness of Biaxin, such as, "Get your patients back in action with Biaxin;" "Highly effective against common respiratory infections;" "Highly effective against common pediatric respiratory infections;" "Penetration and speed of bactericidal activity; etc.," without disclosing any risk information about the product. For example, the posters fail to disclose that Biaxin is contraindicated in patients with a known hypersensitivity to clarithromycin, erythromycin, or any of the macrolide antibiotics; that Biaxin is contraindicated in patients receiving terfenadine,

cisapride, or pimozide who have pre-existing cardiac abnormalities or electrolyte disturbances; that Biaxin should not be used in pregnant women except in circumstances where no alternative therapy is appropriate; and the most common side effects (including rates) associated with the use of Biaxin. These side effects are diarrhea (3%), nausea (3%), abnormal taste (3%), dyspepsia (2%), abdominal pain (2%), and headache (2%) for adults, and diarrhea (6%), vomiting (6%), abdominal pain (3%), rash (2%), and headache (2%) for children. Failure to include this information renders the presentation of promotional messages lacking in fair balance or otherwise misleading.

Misleading Statements

- **"Speed of Bactericidal Activity: Biaxin demonstrated bacterial killing of *B*-lactamase positive *H influenzae* and penicillin-resistant *S pneumonia* within 2-4 hours..."**

  "Speed of Bactericidal Activity: Bactericidal Performance Against *S pneumoniae*"
  "Penicillin-Resistant *S pneumoniae*"

  The above statement(s) that appear on either posters #709-023-1559E, 801-010-2346E, leaflet 712-010-2048, Abbott's home page, or the lunch box are misleading because they imply a greater efficacy for Biaxin than supported by substantial evidence. Specifically, the above statements imply that Biaxin has clinical activity against penicillin-resistant *S pneumonia*. The general focus of the posters is the proven clinical efficacy of Biaxin in pediatric infections (acute otitis media, pneumonia, pharyngitis/tonsillitis, and acute maxillary sinusitis). However, Biaxin is not indicated to treat penicillin-resistant *S pneumonia* associated with any pediatric or adult infection.

  Although Abbott provides the disclaimer that "*In vitro* data are available, but the clinical significance is unknown," this disclaimer is insufficient to correct the misleading impression that Biaxin is clinically effective against penicillin-resistant *S pneumonia*.

  Further, the phrase "speed of bactericidal activity" would be misleading because it implies that Biaxin's efficacy is time dependent and that its "speed of bactericidal activity" enhances its clinical activity and therefore, its effectiveness. Biaxin is a macrolide antibiotic. Pharmacokinetic and pharmacodynamic experience with macrolides and their clinical activity demonstrate that the efficacy of macrolide antibiotics is concentration dependent and not time dependent. Therefore, Biaxin's speed of bactericidal activity would not be clinically relevant.

Finally, bactericidal activity is achieved when reduction in bacterial counts has reached 3 logs (by definition). Biaxin's *in vitro* bacterial killing (reduction) for *B*-lactamase-positive *H influenzae* and penicillin-resistant *S pneumoniae* and is 1 log at 2 hours and 2 logs & 1 log at 4 hours respectively. Biaxin's 3 logs reduction in bacterial killing (reduction) is achieved at 5 hours for *B*-lactamase-positive *H influenzae* and at 10 hours for penicillin-resistant *S pneumoniae*. Therefore, the above statement is false or misleading without substantial evidence for support.

In order to address these violations, DDMAC recommends that Abbott take the following actions.:

1. Immediately discontinue the use of the aforementioned materials and any other promotional materials for Biaxin that contain the same or similar presentations; and

2. Provide a written response to DDMAC of your intent to comply with the above request, and a list of promotional materials containing the misleading presentations that will be discontinued.

Abbott's response should be received no later than 10 business days from the issue date of this letter. If Abbott has any questions or comments, please contact the undersigned by facsimile at (301) 594-6771, or at the Food and Drug Administration, Division of Drug Marketing, Advertising and Communications, HFD-40, Rm 17B-20, 5600 Fishers Lane, Rockville, MD 20857.

DDMAC reminds Abbott that only written communications are considered official.

In all future correspondence regarding this particular matter, please refer to MACMIS ID #6851 in addition to the NDA number.

Sincerely,

Jo Ann Spearmon, M.P.A., Pharm.D.
Regulatory Review Officer
Division of Drug Marketing,
Advertising and Communications