DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

AUG 14 1997

**TRANSMITTED VIA FACSIMILE**

Jennifer L. Stotka, M.D.
Director
U.S. Regulatory Affairs
Eli Lilly and Company
Lilly Corporate Center
Indianapolis, IN 46285

**RE: NDA # 50-667**
**Lorabid (loracarbef)**
**MACMIS ID # 5638**

Dear Dr. Stotka:

Reference is made to Eli Lilly and Company's (Lilly) March 3, 1997, submission of promotional materials under cover of FDA Form 2253 for Lorabid (loracarbef). This submission included brochure # 60-LO-0637. The Division of Drug Marketing, Advertising and Communications (DDMAC) has reviewed this promotional piece and finds it in violation of the Federal, Food, Drug, and Cosmetic Act and the applicable regulations. Specifically, DDMAC objects to the following:

**"Lorabid Covers the Key Pathogens"**

The graphic presentations and statements accompanying this claim are misleading because they imply that Lorabid is superior to Cefzil in treating otitis media caused by *Streptococcus pneumonia* & *Hemophilus influenzae* without substantial evidence for support.

Specifically, the presentations compare the middle ear fluid level for Lorabid and Cefzil and the $MIC_{90}$ values for these products against *S pneumonia* and *H influenzae*:

- One presentation states that the $MIC_{90}$s for loracarbef for *S pneumonia* (including penicillin intermediate-resistant strains) and *H influenzae* (*B*-lactamase +/-) are 2.0*u*g/ml and 0.5*u*g/ml respectively.

- Another presentation states that the $MIC_{90}$s for cefprozil for *S pneumonia* (including penicillin intermediate-resistant strains) and *H influenzae* (*B*-lactamase +/-) are 0.5*u*g/ml and 16*u*g/ml respectively.

The presentations are accompanied by the statements "Lorabid: Middle ear fluid levels exceeded key $MIC_{90}$s in most patients;" and "Cefzil: Middle ear fluid levels often fell short," and imply a greater efficacy or superiority for Lorabid over Cefzil. These presentations provide data for Lorabid and Cefzil that are not derived from adequate and well-controlled head-to-head clinical studies. Although Lilly provides a disclaimer that states "Therapeutic efficacy cannot be predicted by the concentrations attained in a specific body fluid or tissue," this disclaimer is insufficient to balance the implied claim that Lorabid is superior to Cefzil in treating otitis media due to *S pneumonia & H influenzae*.

The use of pharmacokinetic data and MIC data from different studies and the presentation of statements that imply a greater efficacy or superiority for Lorabid in treating otitis media due to *S pneumonia* or *H influenzae* are misleading, when such has not been demonstrated by adequate, well-controlled head-to-head clinical studies. In addition, Lilly's tagline "real-life efficacy patients can feel good about" is misleading because it implies that the comparative studies referenced in this brochure are a valid comparison of the two products.

- **False Indication**

The graphic presentation that provides the cost comparisons and indications for Cefzil & Lorabid is misleading because it fails to reveal material facts concerning the indication for Cefzil in treating sinusitis. Specifically, the presentation gives the drug cost for Lorabid in treating bacterial infections of acute bronchitis, acute bacterial exacerbations of chronic bronchitis and sinusitis. The graphic presentation does not state that Cefzil is indicated to treat sinusitis.

Cefzil is a broad-spectrum cephalosporin antibiotic that is indicated to treat acute sinusitis caused by *S pneumoniae, H influenzae* (including *B*-lactamase producing strains), and *Moraxella catarrhalis* (including *B*-lactamase producing strains). This product indication information is included in the approved

product labeling (PI) for Cefzil. Consequently, by omitting relevant indication information for Cefzil in treating sinusitis, Lilly is implying a greater utility for Lorabid. Thus, this presentation is misleading.

In order to address these objections, DDMAC recommends that Lilly take the following actions:

1. Immediately discontinue the use of the brochure and any other promotional materials for Lorabid that contain the same or similar claims.

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.

Lilly's response should be received no later than August 25, 1997. If Lilly 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.

In all future correspondence regarding this particular matter, please refer to MACMIS ID # 5638 in addition to the NDA number.

Sincerely,

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