DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NOV 25 1997

TRANSMITTED VIA FACSIMILE

Barbara A. Thompson
Assistant Director, Advertising Policy
Regulatory Affairs
GlaxoWellcome
5 Moore Drive, P.O. Box 13398
Research Triangle Park, NC 27709

RE: NDA # 20-695
Raxar (grepafloxacin hydrochloride) Tablets
MACMIS ID # 6034

Dear Ms. Thompson:

Reference is made to GlaxoWellcome's (Glaxo) November 6, 1997, press release regarding Raxar Tablets. The Division of Drug Marketing, Advertising and Communications (DDMAC) has reviewed this press release and finds it to be in violation of the Federal Food, Drug, and Cosmetic Act and the applicable regulations. Specifically, DDMAC objects to the following:

The press release is misleading because it contains a claim related to the mechanism or site of action that is not supported by substantial evidence. Specifically, the statement "Raxar provides targeted coverage against the common respiratory bacteria..." is misleading because it implies that Raxar preferentially accumulates only at the infection site, e.g. the respiratory tract.

The press release is also misleading because it presents comparative *in vitro* data that implies clinical superiority for Raxar against respiratory bacteria over other anti-infective products without substantial evidence for support. Specifically, the press release states that the results of an *in vitro* study showed that Raxar provided activity against nearly 100% strains of *Streptococcus pneumoniae* that were resistant to penicillin and clarithromycin. In addition, the study states that no other antibiotic tested in the study had greater activity against penicillin-resistant *S pneumoniae* than grepafloxacin. The anti-infective products tested in this *in vitro* study included amoxicillin, clarithromycin, azithromycin, ciprofloxacin and levofloxacin.

However, the results of clinical studies used as the basis of approval for Raxar, in the treatment of respiratory infections, e.g. acute bacterial exacerbations of chronic

bronchitis and pneumonia, showed that Raxar demonstrated equivalence to the comparator drugs, e.g. amoxicillin and ciprofloxacin. Additionally, the approved product labeling (PI) for Raxar states that Raxar has been shown to be active, both *in vitro* and in clinical infections, against *S pneumoniae* (penicillin-susceptible strains). Raxar is not indicated to treat penicillin-resistant strains of *S pneumoniae*.

Glaxo provides a disclaimer that states "Although *in vitro* data is a useful guide, clinical trial outcomes with grepafloxacin did not always correlate with *in vitro* study results." This disclaimer is not sufficient to correct the misleading impression that Raxar is superior to amoxicillin, clarithromycin, azithromycin, ciprofloxacin and levofloxacin in treating respiratory infections.

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

1. Immediately discontinue the use of all promotional materials for Raxar that contain the same or similar violations.

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 presentation(s), that will be discontinued.

Glaxo's response should be received no later than December 9, 1997. If Glaxo 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 # 6034 in addition to the NDA number.

Sincerely,

/s/
JoAnn Spearmon, Pharm.D., M.P.A.
Regulatory Review Officer
Division of Drug Marketing,
Advertising and Communications