DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

FOI

JUN 27 1997

**TRANSMITTED VIA FACSIMILE**

Michael E. Sliwoski, M.S.
PPD Regulatory Affairs, Advertising
Abbott Laboratories
100 Abbott Park Road
Abbott Park, IL 60064-3500

**RE: NDA# 20-471**
Zyflo (zileuton) Tablets
MACMIS ID# 5424

Dear Mr. Sliwoski:

This letter concerns promotion of Zyflo (zileuton) Tablets. It has come to the attention of the Division of Drug Marketing, Advertising, and Communications (DDMAC) that Abbott may be promoting claims for Zyflo that are false, misleading, or otherwise lacking in fair balance in violation of the Federal Food, Drug, and Cosmetic Act (Act) and its implementing regulations.

I. Abbott Press Release Promoting Unapproved "Step-Down" Dosage Labeling Regimen

DDMAC has reviewed a May 5, 1997, press release (704-35V-9753) disseminated by Abbott Laboratories entitled, "Abbott Laboratories Requests Dosage Labeling Change for Zyflo (zileuton)--Study Shows Some Asthma Patients Maintained With Fewer Doses." DDMAC has determined that this press release (i.e., promotional labeling) contains conclusory statements about Zyflo efficacy based on a "step-down" dosage study that Abbott has submitted for FDA review as a supplemental new drug application. These statements include:

- "Results from this study suggest some patients who are well controlled with 600 milligrams of Zyflo four times daily may be able to take fewer doses of Zyflo and still maintain asthma symptom control."

- "We are pleased to learn that some patients may be able to reduce the number of daily doses of Zyflo once controlled at currently indicated doses."

FDA has not yet reviewed the submitted study design and data or rendered a decision on the adequacy of the step-down dosing data to support such labeling claims. Thus, any implied or suggested conclusions of Zyflo efficacy based on reduced dosing have not yet been adequately

demonstrated. Therefore, DDMAC considers the above statements and any similar statement of implied drug efficacy based on step-down dosing to be inconsistent with the approved product labeling for Zyflo and to be promotion of an unapproved use in violation of the Act. Abbott should cease the dissemination of this press release and similarly violative materials immediately.

II. Violative "Homemade" Promotions by Abbott Sales Force

DDMAC has received information about various promotional claims, including unapproved Zyflo dosage regimens (i.e., step-down dosing) and unsubstantiated efficacy claims, allegedly being disseminated by Abbott sales representatives in widely varied geographic areas of the United States, as illustrated by the list of enclosed copies of Zyflo sample packages and promotional labeling:

1. Zyflo sample package, Alabama
2. Zyflo sample package, Wyoming
3. Top of a Zyflo sample package, Alabama
4. Zyflo "slim jim", Florida
5. Zyflo "slim jim", New York
6. Zyflo "slim jim", Indiana, including Abbott sales representative's name
6. "Zyflo is cost-effective" piece, Iowa
7. Zyflo label, with handwritten note to promote use in exercise-induced asthma, Iowa
8. "Zyflo Patient Types (Which patients should receive Zyflo)", Ohio
9. "Zyflo vs Accolate" comparative product attribute charts, implying cross-comparison studies performed, Puerto Rico, Arkansas, Iowa, and North Dakota, respectively.

In light of these promotional activities that Abbott representatives may be responsible for, DDMAC requests that you provide a written response to the following questions and request for information:

a) What knowledge does Abbott have concerning the handwritten step-down dosing information placed on Zyflo materials, including Zyflo sample packages?

b) What involvement did Abbott's employees, including its sales force, have in developing and disseminating "homemade" promotional Zyflo materials such as those listed above?

c) Describe all information that Abbott provided its sales force related to the statements used in the materials such as those listed above. This should include (1) written instructions on the use of these materials, and (2) verbal instructions on the use of these materials.

DDMAC requests that you provide a written response by July 14, 1997 answering the above questions and outlining a plan of action addressing the two issues outlined above. Please submit your response to 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 17-B-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 #5424 in addition to the NDA number.

Sincerely,

Joan Hankin

Joan Hankin, JD
Regulatory Review Officer
Division of Drug Marketing,
Advertising, and Communications

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