DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

FDA

Food and Drug Administration
Rockville MD 20857

MAY 20 1998

TRANSMITTED VIA FACSIMILE

Ms. Donna M. Dea
Assistant Manager, Marketed Products Group
Drug Regulatory Affairs Department
Zeneca Pharmaceuticals
1800 Concord Pike
P.O. Box 15437
Wilmington, DE 19850-5437

RE: NDA# 20-547
Accolate (zafirkulast) Tablets
MACMIS ID# 6483

Dear Ms. Dea:

As part of its routine monitoring activities, the Division of Drug Marketing, Advertising, and Communications (DDMAC) has reviewed promotional materials for Accolate (zafirkulast) Tablets (e.g., brochure AC1127 - 298) and has determined that these materials are false or misleading and therefore violate the Federal Food, Drug, and Cosmetic Act and its implementing regulations.

DDMAC has reviewed these materials and determined that they contain an unsubstantiated critical primary efficacy endpoint (FEV1), misleading selective presentation or "cherry-picking" of quality of life (QoL) data, and unsubstantiated asthma-specific quality of life claims for Accolate:

- "Accolate was shown to improve patients' quality of life in a 13-week trial"
- "Accolate--significant improvements seen in these important quality of life measures"
- "Patients taking Accolate experienced statistically significant improvements from screen to endpoint in all four quality of life (QoL) domains... and in overall QoL parameters"

Because of various flaws in the design and conduct of the study (9188IL/0086), the cited data do not substantiate any QoL claims in Accolate promotional materials.

Even if the study design were not flawed for all of the reasons discussed above, the presentation of the QoL data in the cited brochure is still misleading because it "cherry-picks" the "best result" domains in the bar graph, and these data do no provide adequate evidence that use of Accolate over placebo results in a clinically significant benefit as measured

Zeneca should immediately cease its use of promotional materials that contain these or similar claims or representations. Zeneca should respond in writing by June 4, 1998, including a list of all similarly violative materials and a description of its method for discontinuing their use.

Zeneca's response should be directed 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 Zeneca that only written communications are considered official.

In all future correspondence regarding this particular matter, please refer to MACMIS# ID 6483 in addition to the NDA number.

Sincerely,

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