DEPARTMENT OF HEALTH & HUMAN SERVICES

FOI

Food and Drug Administration
Rockville MD 20857

TRANSMITTED VIA FACSIMILE

JUN 14 1999

Ms. Mary Jane Nehring
Director, Marketed Products Support
Worldwide Regulatory Affairs
Schering Corporation
2000 Galloping Hill Road
Kenilworth, NJ 07033

RE: NDA# 17-573
Vanceril 42 mcg (beclomethasone dipropionate) Inhalation Aerosol
MACMIS ID# 7436

Dear Ms. Nehring:

As part of its monitoring and surveillance program, the Division of Drug Marketing, Advertising, and Communications (DDMAC) has reviewed a detail aid directed to health care professionals for Vanceril 42 mcg (beclomethasone dipropionate) ("BDP") Inhalation Aerosol (VDN0016/22208101 "The facts about Singulair from Merck", 10/98). This promotional labeling counterdetails Singulair (montelukast sodium) Tablets by reproducing excerpted pages from a Singulair launch detail aid and providing promotional written commentary about data comparing Singulair to a non-U.S. formulation of inhaled BDP, rather than to Vanceril brand of BDP. DDMAC has concluded that this Vanceril detail aid lacks fair balance and contains false or misleading claims and is therefore violative of the Federal Food, Drug, and Cosmetic Act and implementing regulations.

Overall Misleading Presentation and Use of Inappropriate Comparator

The overall presentation of this Vanceril detail aid is misleading. This piece does not clearly and prominently identify itself as a promotion for Vanceril brand (beclomethasone dipropionate) Inhalation Aerosol. Rather, the front cover "The facts about Singulair from Merck" misleadingly implies that this piece was developed by Merck and Co., Inc. The only corporate source of identification on this promotional piece is the logo for Key Pharmaceuticals, Inc. (Schering's marketing arm) on the bottom of the last page.

Moreover, the Vanceril detail aid relies on an inappropriate BDP comparator to base its comparisons to Singulair. Based on data in the Singulair approved product labeling, all of the comparisons excerpted from the Singulair detailer appearing in this Vanceril piece are between Singulair and a non-U.S. formulation of inhaled BDP. However, because of formulation-related

issues concerning dosing and relative safety and efficacy, Schering has inappropriately substituted Vanceril, a U.S. formulation of BDP, for the non-US formulation of BDP originally studied with Singulair. Although the Vanceril detailer's claims using "BDP" are asterisked to a footnote, "The BDP used in this study was not Vanceril brand of beclomethasone dipropionate", this statement is neither prominently disclosed, nor adequate to remedy the overall misleading impression that the data for Vanceril (a U.S. formulation of BDP) provides the basis for Schering's promotion against Singulair.

Misleadingly Selective and Inappropriate Data Comparison Excerpted From Singulair NDA

In the Vanceril piece, Schering comments on claims excerpted from the Singulair detailer about the addition of Singulair to patients who were not controlled on inhaled BDP alone for the 16-week treatment period: "Over last 10 weeks of study, no significant difference between combined therapy and BDP* alone in daytime and nighttime symptoms"[1]. This Vanceril claim is inappropriate and misleading because Schering references the Singulair NDA to describe an analysis of a 10-week period that was not intended to compare BDP monotherapy to BDP+Singulair (combination therapy) after the 16-week treatment period. This last 10 weeks' analysis was designed to compare Singulair versus placebo after BDP had been withdrawn to allow for a washout of the BDP treatment effect. Schering's misleadingly selective reference from the Singulair NDA promotes an inappropriate and unfavorable analysis that was never designed to compare the BDP+Singulair combination therapy to BDP monotherapy.

Undefined Clinical Endpoints Promote Misleading Superiority Claims

In the Vanceril piece, Schering misleadingly promotes "BDP" superiority by making comments on the excerpted Singulair launch graph that shows time course to first "asthma attack" (as explicitly defined by Merck) between Singulair, BDP, and placebo: "With BDP*, fewer exacerbations, more asthma-free days"[1] (the BDP used in this study was not Vanceril). These BDP superiority claims are misleading because they do not describe the graph endpoint (time course to first "asthma attack") accurately. In addition, although these claims are referenced to the Singulair NDA, they are misleading because they do not define "exacerbations" or "asthma-free days", specifically defined terms according to Merck study protocols. Furthermore, since Merck revised the endpoint "asthma-free days" to "asthma-control days" from the original study protocol and NDA submission, neither the Singulair prescribing information, nor any of Merck's promotional pieces for Singulair even use the term "asthma-free days." Therefore, promotion of such undefined endpoints is misleading to clinicians who might not apply a consistent definition of such terms, and since these endpoints could appear to be derived from the Singulair graph of time course to first "asthma attack."

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1 Data on File Merck Research Laboratories, NDA 20-829 Singulair montelukast tablets: February 21, 1997.

False or Misleading Claim is Inconsistent with Vanceril Indication

One claim on the last page of the Vanceril piece that promotes inhaled corticosteroids as a class states, "[h]elp control the inflammation that may lead to irreversible lung damage." This claim is inconsistent with the approved indication for Vanceril, promotes an off-label indication, and is therefore false or misleading. Schering has been advised of this issue in previous DDMAC correspondence (DDMAC letters dated August 24, 1998; December 9, 1998; and December 21, 1998; and May 6, 1999).

Lack of Fair Balance

The promotional piece for Vanceril lacks fair balance despite making various claims for inhaled corticosteroids including beclomethasone dipropionate versus Singulair, throughout the piece. The promotional piece does not contain any risk information associated with Vanceril 42 mcg.

Schering should immediately cease its use of Vanceril 42 mcg or Vanceril 84 mcg promotional materials or activities that contain these or similarly violative claims. Schering should respond in writing no later than June 28, 1999, describing its commitment to cease use of these materials or activities, include a list of materials containing similarly violative claims, and describe its plan to ensure that its agents, including its sales force, cease further false or misleading safety and efficacy claims.

Your 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. We remind Schering that only written communications are considered official.

In all future correspondence regarding this particular matter, please refer to MACMIS ID# 7436 in addition to the NDA number.

Sincerely,

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