DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville MD 20857

MAY - 9 2000

TRANSMITTED VIA FACSIMILE

C. Elaine Jones, Ph.D.
Product Director, Regulatory Affairs
Glaxo Wellcome Inc.
5 Moore Drive
P.O. Box 13398
Research Triangle Park, NC 27709

Re: NDA# 20-548
Flovent (fluticasone propionate) Inhalation Aerosol
44 mcg, 110 mcg, 220 mcg
MACMIS ID#: 8868

Dear Dr. Jones:

This letter concerns professional and direct-to-consumer promotional materials and advertisements for Flovent (fluticasone propionate) 44 mcg and 110 mcg Inhalation Aerosol disseminated by Glaxo Wellcome Inc (GW) (e.g., pharmacist letter FLO67R0, April 2000). The Division of Drug Marketing, Advertising, and Communications (DDMAC) has reviewed these pieces and concluded that GW is disseminating promotional materials that contain a misleading clinical superiority claim. This claim violates the Federal Food, Drug, and Cosmetic Act and implementing regulations and should be discontinued immediately.

These presentations suggest that asthma patients who are being treated with inhaled corticosteroids (ICSs), including any out-of-stock beclomethasone dipropionate (BDP) inhalation aerosol product (i.e., Vanceril 42 mcg or 84 mcg Inhalation Aerosol), should consider being switched to Flovent because, among other reasons, it is "the number one prescribed (branded)[1] inhaled anti-inflammatory asthma medication in the world" and because *"Flovent has been proven superior to Beclovent (beclomethasone dipropionate) Inhalation Aerosol in improving lung function by FEV_1.*[2]"

The Beclovent comparison is a misleading global clinical superiority claim and suggests that Flovent is the best ICS choice for asthma controller therapy. However, it is misleading to

1 Those promotional materials that omit the qualifier "brand" in the "most prescribed" claim are misleading.
2 Raphael GD, Lanier RQ, Baker J, et al. A comparison of multiple doses of fluticasone propionate and beclomethasone dipropionate in subjects with persistent asthma." *J Allergy Clin Immunol.* 1999;103:796-803.

suggest that Flovent is superior to all BDP products based on data comparing only Beclovent brand BDP Inhalation Aerosol at 42 mcg per puff because other BDP products vary by formulation and dosage strength. Moreover, it misleading to suggest that Flovent is superior to Beclovent regardless of how each product is dosed. The study trials did not demonstrate that Flovent was more efficacious than Beclovent on a microgram-versus-microgram basis for measuring FEV_1. There was no consistent replication of the superiority of the individual doses of Flovent against the individual doses of Beclovent, nor did the trials demonstrate that Flovent had superior "lung function" based on secondary efficacy endpoints (PEFRs and PVC). Therefore, the suggestion of Flovent's global superior efficacy is unsubstantiated and misleading.

Furthermore, this global "proven superior" claim suggests a better therapeutic ratio for Flovent compared to Beclovent by making inferences about relative safety. However, the trials did not measure systemic safety (e.g., HPA-axis suppression) between Flovent and Beclovent. Without valid comparative systemic safety assessments, it is misleading to suggest a superior safety profile between these products based only on adverse events. Therefore, the suggestion of global superiority based on Flovent's better benefit-to-risk ratio is unsubstantiated and misleading.

On April 29 and June 9, 1998, DDMAC raised each of these issues to GW in written comments on a preliminarily proposed Flovent presentation that were based in part on these study data.

GW should immediately cease its dissemination and use of all promotional materials for Flovent with this misleading global superiority claim. We should receive your written response no later than May 23, 2000, and it should list all similarly violative materials, with a description of your method of discontinuation. 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-42, Rm 17-B-20, 5600 Fishers Lane, Rockville, Maryland 20857. We remind GW that only written communications are considered official.

In future correspondence regarding this particular matter, please refer to MACMIS ID# 8868 in addition to the NDA number.

Sincerely,

/S/

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

GlaxoWellcome

April 3, 2000

Attention Pharmacist:

As you may know, Schering Laboratories announced on March 29, 2000 that it was voluntarily recalling certain inhaled beclomethasone dipropionate medications. The products involved in the recall are from certain lots manufactured prior to September 30, 1999 and include Vanceril®* (beclomethasone dipropionate, 42 mcg) Inhalation Aerosol, and Vanceril® 84 mcg Double Strength (beclomethasone dipropionate, 84 mcg) Inhalation Aerosol.†

If your customers are unable to replace their medications affected by the recall with the same medication, we would like you to consider switching these patients to an effective alternative, FLOVENT® (fluticasone propionate) Inhalation Aerosol 44 mcg and 110 mcg, and want you to know that FLOVENT is readily available.

Here are several reasons to consider FLOVENT Inhalation Aerosol:

- FLOVENT is the number one prescribed inhaled anti-inflammatory brand in the world.[1]
- FLOVENT offered superior improvement vs. BECLOVENT* (beclomethasone dipropionate, USP) Inhalation Aerosol in lung function as measured by FEV_1.[2]
- FLOVENT has no HPA-axis suppression at recommended dosages of up to 440 mcg per day.
- FLOVENT 44 mcg offers a lower daily cost than BECLOVENT, Vanceril, and Azmacort*.†§[3]

THERAPY	PUFFS/DAY	COST/DAY
FLOVENT 44 mcg	2 puffs b.i.d.	$1.56[3]
FLOVENT 110 mcg	2 puffs b.i.d.	$2.07[3]

- FLOVENT has convenient twice-daily dosing – may help compliance.
- FLOVENT Inhalation Aerosol is indicated for the maintenance treatment of asthma as prophylactic therapy for patients 12 years of age and older.

FLOVENT is NOT indicated for the relief of acute bronchospasm. CAUTION: Adrenal insufficiency may occur when transferring patients from systemic steroids (see WARNINGS in complete Prescribing Information). Commonly reported adverse events in patients receiving FLOVENT Inhalation Aerosol up to 110 mcg, 2 puffs b.i.d. (and placebo) were headache 17%–22% (14%), upper respiratory infection 15%–22% (12%), nasal congestion 8%–16% (8%), pharyngitis 10%–14% (7%), influenza 3%–8% (2%), and sinusitis 3%–6% (4%).

*Vanceril is a registered trademark of Schering Corporation.
†More information about the recall and the products affected can be found at www.rxrecall.net.
‡Based on average wholesale price, *Medi-Span*®. December 1999. Actual prices paid by healthcare institutions or individual payers may differ. Comparable efficacy among these products has not been established.
§Azmacort is a registered trademark of Rhône-Poulenc Rorer Pharmaceuticals Inc.

References: 1. Source™ Prescription Audit (SPA), Asthma market: inhaled corticosteroids, July 1999, Scott-Levin, Inc. 2. Raphael GD, Lanier RQ, Baker J, et al. A comparison of multiple doses of fluticasone propionate and beclomethasone dipropionate in subjects with persistent asthma. *J Allergy Clin Immunol.* 1999;103:796–803. 3. *Medi-Span.* December 1999.

Please consult accompanying complete Prescribing Information.

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