PUBLIC ADVISORY
Health Canada Endorsed Important Safety Information on RITONAVIR and FLUTICASONE PROPIONATE

Subject : Information for patients regarding a drug interaction between ritonavir (NORVIR®/KALETRA®) and fluticasone propionate (FLONASE®, FLOVENT®, ADVAIR®)

MISSISSAUGA, Ontario (January 27, 2004) – GlaxoSmithKline Inc. is informing patients of the results of a drug interaction study conducted with FLONASE® (fluticasone propionate) aqueous nasal spray and NORVIR® (ritonavir, Abbott Laboratories).

A recent clinical study in healthy volunteers found that concurrent administration of NORVIR® (ritonavir, Abbott Laboratories) and FLONASE® (fluticasone propionate, GlaxoSmithKline) aqueous nasal spray, an intranasal corticosteroid for allergies, resulted in greatly increased concentrations of fluticasone propionate in the blood. In addition, GlaxoSmithKline has received reports of adrenal suppression in patients who were taking ritonavir and fluticasone propionate simultaneously. Adrenal suppression is a condition in which the adrenal glands produce too little of the hormones required for the body's normal functioning, reducing the body's ability to heal, particularly after surgery, infection or serious injury. Therefore, ritonavir and fluticasone should only be taken together if the benefit to the patient outweighs the risk of adrenal suppression. Care should also be taken for patients who are taking other drugs that are known to affect fluticasone propionate metabolism, such as azole antifungals.

Ritonavir, a protease inhibitor used in the treatment of HIV/AIDS, is a potent inhibitor of the enzymes responsible for elimination of fluticasone propionate from the body. When taken together with some inhaled or intranasal corticosteroids, patients may be at risk of corticosteroid side effects, such as adrenal suppression. Inhaled or intranasal corticosteroids are used to treat allergies, asthma, and/or chronic obstructive pulmonary disease (COPD).

Other corticosteroid preparations are known to share the same elimination pathway as fluticasone propionate and could potentially be affected by the interaction with ritonavir, resulting in adverse

events similar to that seen with fluticasone propionate. **HIV-infected patients who are also taking a corticosteroid preparation should contact their physician to discuss their current medications.**

Patients are advised that medications should not be stopped without consulting a physician. Abruptly stopping medications may result in deteriorating health, which may be life-threatening.

Fluticasone propionate is also contained in the products FLOVENT® (fluticasone propionate) inhalation aerosol and dry powder for inhalation, and ADVAIR® (salmeterol xinafoate/fluticasone propionate) inhalation aerosol and dry powder for inhalation, manufactured by GlaxoSmithKline.

GlaxoSmithKline has sent a letter to health care professionals in Canada informing them of the drug interaction between ritonavir and FLONASE® and of other potential interactions with inhaled or intranasal corticosteroids by the same pathway as fluticasone. This information may be obtained on the Canadian website of GlaxoSmithKline (http://www.gsk.ca/en/) or on the website of the Therapeutic Products Directorate of Health Canada (http://www.hc-sc.gc.ca/hpfb-dgpsa/tpd-dpt/index_advisories_professionals_e.html#2004).

Suspected adverse reactions arising from the simultaneous use of ritonavir and fluticasone propionate can be reported directly to GlaxoSmithKline at the following address:

GlaxoSmithKline Inc.
7333 Mississauga Road N
Mississauga, Ontario
L5N 6L4
Tel: 1-800-387-7374

Any suspected adverse reaction can also be reported to:
Canadian Adverse Drug Reaction Monitoring Program (CADRMP)
Marketed Health Products Directorate
HEALTH CANADA
Address Locator: 0701C
OTTAWA, Ontario, K1A 0K9
Tel: (613) 957-0337 or Fax: (613) 957-0335
To report an Adverse Reaction, consumers and health professionals may call toll free:
Tel: 866 234-2345
Fax: 866 678-6789

For other inquiries: please refer to contact information

The AR Reporting Form and the AR Guidelines can be found on the Health Canada web site or in *The Canadian Compendium of Pharmaceuticals and Specialties*.

http://www.hc-sc.gc.ca/hpfb-dgpsa/tpd-dpt/adverse_e.html
http://www.hc-sc.gc.ca/hpfb-dgpsa/tpd-dpt/adr_guideline_e.html