Health Canada Endorsed Important Safety Information on LAMICTAL® (lamotrigine) Tablets

August 8, 2006

Subject: **Use of LAMICTAL® (lamotrigine) in the first trimester of pregnancy may have an increased risk of cleft lip and/or cleft palate, compared to background rates in the general population**

Mississauga, Ontario (August 8, 2006) -- GlaxoSmithKline Inc. (GSK), following discussions with Health Canada, is informing patients of new safety information concerning the antiepileptic, LAMICTAL® (lamotrigine) tablets.

New data from a pregnancy registry suggest an association between taking LAMICTAL® (lamotrigine) in the first trimester of pregnancy, and increased risk of cleft lip and/or cleft palate in the baby. Such "oral clefts" are a failure of the normal closure of the mouth structures as the unborn baby develops, resulting in a gap in the upper lip and/or the roof of the mouth (i.e. soft or hard palate).

Oral clefts are amongst the most common of the major birth defects occurring in the general population at background rates from 0.5 to 2.16 per 1000 births. There is a genetic aspect, in that an unborn baby with an affected parent or sibling is at increased risk. From the literature, several anti-epileptic drugs have been shown to be associated with oral cleft, and other factors are also suspected, including maternal smoking, heavy alcohol intake, infections, folic acid deficiency, and vitamin A intoxication.

Regarding LAMICTAL®, the ongoing North American Antiepileptic Drug (NAAED) Pregnancy Registry detected an elevated rate of isolated, non-syndromic cleft palate deformity (which means that the cleft lip and/or cleft palate is not accompanied by other major birth defects) occurring in infants exposed to lamotrigine monotherapy during the first trimester of pregnancy, as compared to the reference population used in this Registry. Data from additional pregnancy registries are required in order to get a more complete picture of the risk.

As is currently stated in the product information, patients should notify their physicians if they become pregnant or intend to become pregnant during therapy with LAMICTAL®. Although pregnant woman and their unborn children may face significant health risks from uncontrolled epilepsy, LAMICTAL® should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. Patients should not start or stop these medications without consulting their doctor. Sudden discontinuation of antiepileptic therapy may lead to breakthrough seizures with serious consequences for both the mother and the fetus and should be avoided. Talk with your doctor or pharmacist if you have questions or concerns.

GSK has sent a letter to health-care professionals informing them of this new safety information. This information may be obtained on the Canadian website of GSK http://www.gsk.ca or on the website of the Therapeutic Products Directorate of Health Canada http://www.healthycanadians.gc.ca/recall-alert-rappel-avis/hc-sc/2006/14412a-eng.php. GSK continues to work closely with Health Canada to monitor adverse event reporting and to ensure that up-to-date information regarding the use of lamotrigine is available.

Managing marketed health product-related adverse reactions depends on health-care professionals and consumers reporting them. Reporting rates determined on the basis of spontaneously reported post-marketing adverse reactions are generally presumed to underestimate the risks associated with health

product treatments. Any case of cleft lip and/or cleft palate or other serious or unexpected adverse reactions in patients receiving LAMICTAL® should be reported to GSK, or Health Canada at the following addresses:

GlaxoSmithKline Inc.
7333 Mississauga Road North
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
cadrmp@hc-sc.gc.ca

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/dhp-mps/medeff/report-declaration/form/ar-ei_form_e.html
http://www.hc-sc.gc.ca/dhp-mps/medeff/report-declaration/guide/ar-ei_guide-ldir_e.html

For other inquiries related to this communication, please contact Health Canada at:
Bureau of Cardiology, Allergy and Neurological Sciences
E-mail: BCANS_Enquiries@hc-sc.gc.ca
Tel: (613) 941-1499
Fax: (613) 941-1668

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For media inquiries, please contact Peter Schram, (905) 819-3363.