PUBLIC COMMUNICATION
Health Canada Endorsed Important Safety Information on Paroxetine

December 22, 2005

Subject: **Additional Study Shows Use of Paroxetine in First Trimester of Pregnancy May Have Small Increased Risk of Heart-Related Birth Defects, Compared to Other Antidepressants**

Mississauga, Ontario (December, 2005) — GlaxoSmithKline Inc. (GSK), following discussions with Health Canada, is providing an update on the use of paroxetine during the first trimester of pregnancy. A previous advisory was issued on this subject in October 2005, regarding preliminary results of an epidemiology study sponsored by GSK using a United States database. The results of that analysis suggested there may be a small increase in the risk of birth defects, including heart-related defects, in babies whose mothers were prescribed paroxetine in the first trimester of pregnancy, compared to other antidepressants. This second advisory is being issued as a result of new analysis of Swedish national registry data, which shows similar findings to those of the US study regarding heart-related defects, but unlike the US study, did not find an increased risk of overall birth defects.

- The combined results from two large database studies now suggest that if the mother takes paroxetine in the first trimester of pregnancy, the risk of having a baby with a heart defect increases to approximately 2/100 (2 percent), as compared to approximately 1/100 (1 percent) with other antidepressants, or in the general population. Other antidepressants do not show this increased risk in these studies. Most of the heart-related defects were atrial or ventricular septal defects, conditions in which there are holes in the wall separating the left and right chambers of the heart.
- Doctors have been advised to inform patients of this paroxetine-associated risk to the fetus.
- Pregnant women currently taking paroxetine, who are in their first trimester, and those women who intend to become pregnant, should consult with their doctor about whether to continue taking it. Generally, paroxetine treatment should only be continued if the benefits for the individual patient are thought to outweigh the risks, while also considering the benefits and risks of switching to another treatment option, or stopping treatment altogether.
- Due to the risk of discontinuation symptoms, it is very important that patients do NOT stop taking paroxetine without first consulting with their doctor.
- If treatment for depression is to be started, other treatment options besides paroxetine should be considered for women who intend to become pregnant, or are in their first trimester.

Heart-related defects are one of the most common types of birth defects in the general population, occurring in about 1/100 infants, or 1 percent, regardless of whether the mother is being treated with antidepressants. In general, septal defects can range from those that are mild and repair themselves spontaneously as the child grows up, to those that are more serious and may require surgery. In the general population, the majority of cases are mild; however the severity of the paroxetine-associated septal defects reported in these studies is unknown.

The Canadian prescribing information and consumer information for PAXIL® (paroxetine hydrochloride tablets) and PAXIL CR™ (paroxetine hydrochloride controlled release tablets) currently includes a precaution that paroxetine should be used during pregnancy only if the potential benefit to the patient justifies the potential risk to the fetus. The Product Monograph also includes information related to possible symptoms and complications observed in newborns exposed to paroxetine, or other newer antidepressants, during the third trimester of pregnancy.

GlaxoSmithKline 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 GlaxoSmithKline (http://www.gsk.ca) or on the website of the Therapeutic Products Directorate of Health Canada (http://www.hc-sc.gc.ca/hpfb-dgpsa/tpd-dpt/index_advisories_public_e.html). Following consultation with Health Canada, the Product Monograph for Paxil and Paxil CR will be revised. If patients have questions regarding their current Paxil or Paxil CR prescription, they are asked to contact their doctor or pharmacist.

For media inquiries, please contact Cathy Metson, (905) 819-3363.

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 events are generally presumed to underestimate the risks associated with drug treatments. Any cases of serious or unexpected adverse reactions in patients taking paroxetine should be reported to GlaxoSmithKline 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 reactions can also be reported to:
Canadian Adverse Drug Reaction Monitoring Program (CADRMP)
Marketed Health Products Directorate
HEALTH CANADA
Address Locator: 0701C
OTTAWA, Ontario, K1A OK9
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

For other inquiries, please refer to contact information:

Bureau of Cardiology, Allergy and Neurological Sciences
BCANS_Enquiries@hc-sc.gc.ca
Tel: (613) 941-1499
Fax: (613) 941-1668

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