Subject: Use of Paroxetine in First Trimester of Pregnancy May Have a Small Increased Risk of Birth Defects, Compared to Other Antidepressants

Mississauga, Ontario (October, 2005) — GlaxoSmithKline Inc., following discussions with Health Canada, is informing patients of new safety information regarding the use of paroxetine during the first trimester of pregnancy. Paroxetine is used for relieving the symptoms of depression and anxiety. As a result of this new safety information, GlaxoSmithKline recommends the following:

- **As per the current Consumer Information for paroxetine, women who are currently taking paroxetine and are pregnant, or planning on becoming pregnant, should discuss with their doctor the potential risks and benefits of using paroxetine therapy during pregnancy.**
- **Doctors have been advised of this new safety information, and are encouraged to discuss the risks and benefits of using paroxetine during pregnancy with their patients.**
- **Due to the risk of discontinuation symptoms, it is very important that patients do NOT stop taking paroxetine without first consulting with their doctor.**

Preliminary results of a recent study conducted by GlaxoSmithKline, suggest there may be a small increase in the risk of birth defects, compared to other antidepressants, in babies whose mother took paroxetine in the first trimester of pregnancy. Specifically, increased risk was reported for overall frequency of birth defects, and in the frequency of heart-related defects. Of the heart-related defects reported, the majority were ventricular septal defects (holes in the muscular wall that separates the right and left ventricles of the heart). This is a common type of birth defect that can spontaneously occur, and the vast majority of cases are mild and spontaneously reverse within a few years after birth. The majority of babies born to women taking paroxetine in this study were born healthy. GlaxoSmithKline had posted the results of this study to its Clinical Trials Register where it can be read by anyone with Internet access. The website is http://ctr.gsk.co.uk/welcome.asp. GlaxoSmithKline is conducting additional analysis to further evaluate these preliminary results.

Other independent studies of pregnancy outcome following first trimester exposure to antidepressants, including paroxetine, provide conflicting evidence regarding the possibility of increased risk of birth defects with these medications.

The Product Monograph 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 during the third trimester of pregnancy.

GlaxoSmithKline has sent a letter to healthcare 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 or Alison Steeves, (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