



Health Santé  
Canada Canada

Health Products and Food Branch  
Direction générale des produits de santé et des aliments

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This is duplicated text of a letter from **GlaxoSmithKline Inc.**  
Contact the company for a copy of any references, attachments or enclosures.

**Health Canada Endorsed Important Safety Information on  
PAXIL® (paroxetine)**



May 2004

**Subject: Stronger WARNING for SSRIs and other newer anti-depressants regarding the potential for behavioural and emotional changes, including risk of self-harm. For paroxetine, this replaces the previous interim contraindication.**

Dear Healthcare Professional:

GlaxoSmithKline Inc. (GSK), following discussions with Health Canada, would like to inform you of important safety information regarding the possibility that selective serotonin reuptake inhibitors (SSRIs) and other newer anti-depressants may be associated with behavioural and emotional changes, including risk of self-harm.

The new Class warning incorporated in the product monograph of paroxetine is provided below.

Please note this warning replaces the interim contraindication for Paxil® (paroxetine) issued in July 2003 for patients under 18 years of age with Major Depressive Disorder.

## **POTENTIAL ASSOCIATION WITH THE OCCURRENCE OF BEHAVIOURAL AND EMOTIONAL CHANGES, INCLUDING SELF-HARM.**

### **Pediatrics: Placebo-Controlled Clinical Trial Data**

- **Recent analyses of placebo-controlled clinical trial safety databases from SSRIs and other newer anti-depressants suggest that use of these drugs in patients under the age of 18 may be associated with behavioural and emotional changes, including an increased risk of suicidal ideation and behaviour over that of placebo.**
- **The small denominators in the clinical trial database, as well as the variability in placebo rates, preclude reliable conclusions on the relative safety profiles among these drugs.**

### **Adult and Pediatrics: Additional data**

- **There are clinical trial and post-marketing reports with SSRIs and other newer anti-depressants, in both pediatrics and adults, of severe agitation-type adverse events coupled with self-harm or harm to others. The agitation-type events include: akathisia, agitation, disinhibition, emotional lability, hostility, aggression, depersonalization. In some cases, the events occurred within several weeks of starting treatment.**

**Rigorous clinical monitoring for suicidal ideation or other indicators of potential for suicidal behaviour is advised in patients of all ages. This includes monitoring for agitation-type emotional and behavioural changes.**

### **Discontinuation Symptoms**

**Patients currently taking paroxetine should NOT be discontinued abruptly, due to risk of discontinuation symptoms. At the time that a medical decision is made to discontinue an SSRI or other newer anti-depressant drug, a gradual reduction in the dose rather than an abrupt cessation is recommended.**

It should be noted that a causal role for SSRIs and other newer anti-depressants in inducing self-harm or harm to others has not been established. The possibility of a suicide attempt is inherent in depression and other psychiatric disorders, and may persist until remission occurs. Therefore, high-risk patients should be closely supervised throughout therapy with appropriate consideration to the possible need for hospitalization. The updated warning informs practitioners that all patients being treated with SSRIs and other newer anti-depressants should be rigorously monitored for clinical worsening, or onset/worsening of agitation-type adverse events, or other indicators of potential for suicidal behaviour.

Paroxetine is not indicated for use in the pediatric population, and controlled clinical studies with paroxetine in children and adolescents under 18 years of age with major depressive disorder failed to demonstrate efficacy.

## New Information Added to the Consumer Information Section

The Consumer Information Section of the product monograph has been updated to reflect this new Class warning, and to advise patients that treatment with SSRIs and other newer anti-depressants is most safe and effective when there is good communication with the treating physician about how the patient is feeling.

### Background

In February 2004, a scientific advisory panel set up by Health Canada was asked to provide the clinical practice perspective on the pediatric clinical trial safety data, and the spontaneous post-marketing reports for SSRIs and other newer anti-depressants. The panel agreed that a contraindication was not warranted for these medications, and supported Health Canada's recommendation for stronger warnings, while providing suggestions and comments. The record of proceedings, and other information about the panel, can be found on Health Canada's website at

[http://www.hc-sc.gc.ca/hpfb-dgpsa/tpd-dpt/sap\\_ssri\\_2004-02-20\\_rop\\_e.html](http://www.hc-sc.gc.ca/hpfb-dgpsa/tpd-dpt/sap_ssri_2004-02-20_rop_e.html).

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 paroxetine is available.

The identification, characterization and management of drug-related adverse events are dependent on the active participation of health-care professionals in adverse drug reaction reporting programs. Healthcare professionals are asked to report any suspected adverse reactions in patients receiving PAXIL® and PAXIL CR™ (paroxetine hydrochloride) directly 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

[cadmp@hc-sc.gc.ca](mailto:cadmp@hc-sc.gc.ca)

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/adverse_e.html)

[http://www.hc-sc.gc.ca/hpfb-dgpsa/tpd-dpt/adr\\_guideline\\_e.html](http://www.hc-sc.gc.ca/hpfb-dgpsa/tpd-dpt/adr_guideline_e.html)

Your professional commitment in this regard has an important role in protecting the well-being of your patients by contributing to early signal detection and informed drug use.

Any questions from health care professionals may be directed to Medical Information via GSK Customer service at 1-800-387-7374.

Sincerely,

***original signed by***

Anne Phillips, M.D., FRCPC  
Vice-President, Research & Development and Chief Medical Officer  
GlaxoSmithKline Inc.