IMPORTANT DRUG SAFETY INFORMATION
Until further information is available,
PAXIL® (paroxetine hydrochloride) should
not be used in children and adolescents under 18 years of age

July 2003

Dear Health Care Professional:

GlaxoSmithKline Inc., following discussions with Health Canada, is alerting you to important emerging safety information regarding reports of possible suicide-related adverse events in pediatric patients treated with PAXIL®. The following information will be incorporated into the Product Monograph:

Until further information is available, PAXIL® (paroxetine hydrochloride) should not be used in children and adolescents under 18 years of age (ie. pediatric patients), due to a possible increased risk of suicide-related adverse events in this patient population.

In pediatric patients with Major Depressive Disorder (MDD), PAXIL® is *contraindicated*, due to additional evidence of lack of efficacy.

There is new evidence from three pediatric placebo-controlled trials in MDD of an increased risk of suicidal thinking, suicide attempts or self-harm. The incidence of these events in the PAXIL® group as compared to the placebo group was: 5.3% (20/378) versus 2.8% (8/285), respectively. Some of these events occurred during the tapering-off period of the studies. The three trials also demonstrated that PAXIL® failed to show greater efficacy than placebo in MDD.

Placebo-controlled data from patients with Social Anxiety Disorder (Social Phobia, SAD) also may suggest an increased risk of possible suicide-related adverse events in patients treated with PAXIL®: 2.4% (4/165) versus 0% (0/157) with placebo. Suicide-related adverse events were also reported in the open label enrichment phase of a study in Obsessive Compulsive Disorder (OCD). In view of the well-established comorbidity between depression and other psychiatric disorders, further information is required before the safe use of PAXIL® can be established in SAD or OCD in pediatrics.

In the pediatric clinical trial programme, which included more than 1,000 patients treated with PAXIL®, there were no completed suicides.

Patients currently taking PAXIL® should *not* discontinue treatment abruptly, due to risk of discontinuation symptoms. A gradual reduction in dose under medical supervision is recommended.

Both the UK Department of Health and the FDA recently issued statements regarding the new evidence from placebo-controlled trials of a possible increased risk of suicidal thinking and suicide attempts in children and adolescents under the age of 18 being treated with the drug PAXIL® for depression.

Although PAXIL® is **not** indicated for use in patients under 18 years of age in Canada, Health Canada is aware of off-label use of this drug in the pediatric population.

After consulting with independent experts in child and adolescent psychiatry, and in conjunction with Health Canada, the following guidance is offered in treating patients under 18 years of age:

- PAXIL® should not be prescribed as new therapy for patients under 18 years of age.
- If your patient is being successfully treated with PAXIL®, then the completion of the planned treatment course should be considered as an option in the management of the illness.
- In all other cases, change of treatment should be considered. If the medical decision is made to stop treatment with PAXIL®, **it is very important that the drug not be discontinued abruptly due to risk of discontinuation symptoms**. A gradual reduction in the dose rather than abrupt cessation is recommended whenever possible. If intolerable symptoms occur following a decrease in the dose or upon discontinuation of treatment dose titration should be managed on the basis of the patient's clinical response. Patients should be monitored when discontinuing treatment, regardless of the indication for which PAXIL® is being prescribed.

This new safety information regarding the use of PAXIL® in children and adolescents under the age of 18 years, does not affect the use of PAXIL® in adults at this time.

GlaxoSmithKline Inc. continues to work closely with Health Canada to monitor adverse event reporting and to ensure that up-to-date information regarding the use of PAXIL® 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 programmes. Health care professionals are asked to report any suspected adverse reactions in patients receiving PAXIL® (paroxetine hydrochloride) directly to GlaxoSmithKline Inc. or the Marketed Health Products Directorate.

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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 GlaxoSmithKline 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.

Any suspected adverse reactions can also be reported to:

Canadian Adverse Drug Reaction Monitoring Program (CADRMP)
Marketed Health Products Directorate
HEALTH CANADA
Address Locator: 0201C2
OTTAWA, Ontario, K1A 1B9
Tel: (613) 957-0337 or Fax: (613) 957-0335
Toll free for consumers and health professionals:
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 TPD web site or in *The Canadian Compendium of Pharmaceuticals and Specialties*.