

**Health Canada Endorsed Important Safety Information on
ZOLOFT (sertraline hydrochloride)**



Pfizer Canada Inc.

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H9R 4V2

May 26, 2004

Subject: Stronger WARNING for SSRIs and other newer antidepressants regarding the potential for behavioural and emotional changes, including risk of self-harm

Dear Health Care Professional,

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

The new Class warning incorporated in the Product Monograph of ZOLOFT* (sertraline hydrochloride) capsules is provided below.

**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 antidepressants 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 antidepressants, 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 behavior is advised in patients of all ages. This includes monitoring for agitation-type emotional and behavioural changes.

Discontinuation Symptoms

Patients currently taking sertraline hydrochloride 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 antidepressant 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 antidepressants 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 antidepressants should be rigorously monitored for clinical worsening, or onset/ worsening of agitation-type adverse events, or other indicators of potential for suicidal behaviour.

Sertraline hydrochloride is not indicated for use in the pediatric population.

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 antidepressants 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 antidepressants. 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/dhp-mps/prodpharma/activit/sci-consult/serotonin/sapssri_rop_gcsisrs_crd_2004-02-20_e.html.

Pfizer Canada 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 ZOLOFT (sertraline hydrochloride) is available.

The identification, characterization and management of drug-related adverse events are dependent on the active participation of healthcare professionals in adverse drug reaction reporting programs. Healthcare professionals

are asked to report any suspected adverse reactions in patients receiving ZOLOFT (sertraline hydrochloride) directly to Pfizer Canada Inc. or Health Canada at the following addresses:

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Medical Information
P.O. Box 800
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