The Health Products and Food Branch (HPFB) posts on the Health Canada web site safety alerts, public health advisories, press releases and other notices as a service to health professionals, consumers, and other interested parties. These advisories may be prepared with Directorates in the HPFB which includes pre-market and post-market areas as well as market authorization holders and other stakeholders. Although the HPFB grants market authorizations or licenses for therapeutic products, we do not endorse either the product or the company. Any questions regarding product information should be discussed with your health professional.

Health Canada Endorsed Important Safety Information on ADHD Drugs

May 2006

Subject: **Attention Deficit Hyperactivity Disorder (ADHD) Drugs: Updated and Standardized Labelling Regarding Very Rare Cardiac-Related Adverse Events**

Dear Health Care Professional,

Health Canada wishes to inform you that the prescribing information of *all* drugs indicated for the treatment of ADHD in adults and children, has been updated to include standardized cautionary prescribing information identifying risk factors for cardiac-related adverse events with this class of drugs, and to provide recommendations to reduce these risks. The changes affect the Contraindications, Warnings and Precautions, Dosing recommendations, and Information for the Patient.

This advisory applies to the following drugs, and all products containing these drugs:

Brand Name	***Manufacturer***
ADDERALL XR® (mixed salts amphetamine extended-release)	**Shire BioChem Inc.**
ATTENADE™ (dextromethylphenidate)	**Biovail Pharmaceuticals Canada** *[approved, but the manufacturer has not marketed in Canada]*
BIPHENTIN® (methylphenidate controlled release)	**Purdue Pharma** *[approved, but the manufacturer has not marketed in Canada]*
CONCERTA* (methylphenidate extended release)	**Janssen-Ortho Inc.**
DEXEDRINE® (dextroamphetamine)	**GlaxoSmithKline Inc.**
RITALIN® (methylphenidate)	**Novartis Pharmaceuticals Canada Inc.**
RITALIN SR® (methylphenidate extended release)	**Novartis Pharmaceuticals Canada Inc.**
STRATTERA® (atomoxetine)	**Eli Lilly Canada Inc.**

*Trademark used under licence to Jannsen-Ortho Inc.

- **ADHD drugs should be started at the lowest possible dose, and increased slowly, as individual patient response to these drugs is known to vary widely.**

- **ADHD drugs should not be used if a patient has: symptomatic cardiac disease; moderate to severe hypertension; advanced arteriosclerosis; or hyperthyroidism.**

- **ADHD drugs should generally not be used in patients with known structural cardiac abnormalities;**

- **Before prescribing an ADHD drug, it is important to be aware of whether the patient: has a family history of sudden death or death related to cardiac problems; participates in strenuous exercise; or takes other sympathomimetic drugs; as these are thought to be additional risk factors. In patients with relevant risk factors, and based on the physician's judgement, further evaluation of the cardiovascular system may be considered before starting on the drug;**

- **Patients who are considered to need long-term treatment with ADHD drugs should undergo periodic evaluation of their cardiovascular status, based on the physician's judgement.**

- **Patients taking drugs for the management of ADHD are being advised not to discontinue their medication without consultation with their physician.**

- **Similar information will appear in the Information for the Patient materials for these drugs.**

Theoretically there exists a pharmacological potential for all ADHD drugs to increase the risk of sudden/cardiac death. All medications for the treatment of ADHD are sympathomimetic. The stimulatory effects from these drugs on the sympathetic nervous system are usually mild or moderate, but in patients of all ages, particularly those with cardiovascular compromise, these effects may result in serious adverse events including sudden/cardiac death. Reports of these serious adverse events are very rare.

In patients treated with ADHD drugs, neither clinical studies nor post-marketing reports have shown to date that the incidence or reporting rates of serious cardiac adverse events, including fatalities, are greater than background rates. Additionally, there is no evidence to show that, in terms of cardiac risk, any one of the drugs indicated for the management of ADHD is better or worse than the others. There is ongoing international discussion about the best way to design clinical studies to further investigate these issues.

Additional information on ADHD Drugs and Cardiac Adverse Events

- A 2004 Food and Drug Administration (FDA) report on sudden death and serious heart problems associated with ADHD drugs is available online at:
  http://www.fda.gov/ohrms/dockets/ac/06/briefing/2006-4202B1_05_FDA-Tab05.pdf

- A Health Canada issued Advisory informing Canadians of the February 2005 suspension of ADDERALL XR® from the Canadian market due to concerns of serious cardiac adverse events can be viewed at:
  http://hc-sc.gc.ca/ahc-asc/media/advisories-avis/2005/2005_01_e.html

- The report and recommendations of Health Canada's New Drug Committee, struck in July 2005, to review the decision to suspend ADDERALL XR® from the Canadian market, and the August 2005 Health Canada announcement of the reinstatement of ADDERALL XR® can be viewed at:
  http://www.hc-sc.gc.ca/dhp-mps/alt_formats/hpfb-dgpsa/pdf/prodpharma/ndca_rep_cnma_rap_2005-08-25_e.pdf
  http://www.hc-sc.gc.ca/ahc-asc/media/nr-cp/2005/2005_92_e.html

- Background material and meeting information on the February 2006 meeting of the FDA's Drug Safety and Risk Management Advisory Committee to discuss approaches to study cardiovascular risks associated with ADHD drugs can be viewed at:
  http://www.fda.gov/oc/advisory/accalendar/2006/cder12535dd02091006.html

- Background material and meeting information on the March 2006 meeting of the FDA's Paediatric Advisory Committee to update and discuss adverse events, including cardiac adverse events, associated with the use of ADHD drugs can be viewed at:
  http://www.fda.gov/oc/advisory/accalendar/2006/fda12604d032206.html

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 reactions are generally presumed to underestimate the risks associated with health product treatments. Any serious or unexpected adverse reactions in patients receiving any ADHD drug should be reported to Health Canada at the following addresses:

Any suspected adverse reaction can 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
cadrmp@hc-sc.gc.ca

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/dhp-mps/medeff/report-declaration/form/ar-ei_form_e.html
http://www.hc-sc.gc.ca/dhp-mps/medeff/report-declaration/guide/ar-ei_guide-ldir_e.html

For other inquiries related to this communication, please contact Health Canada at:
Bureau of Cardiology, Allergy and Neurological Sciences
BCANS_Enquiries@hc-sc.gc.ca
Tel: (613) 941-1499
Fax: (613) 941-1668

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