

# WHO PHARMACEUTICALS NEWSLETTER



prepared in collaboration with the  
WHO Collaborating Centre for  
International Drug Monitoring,  
Uppsala, Sweden

*The aim of this Newsletter is to disseminate information on the safety and efficacy of pharmaceutical products, based on communications received from our network of "drug information officers" and other sources such as specialized bulletins and journals, as well as partners in WHO. The information is produced in the form of résumés in English, full texts of which may be obtained on request from:*

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*This Newsletter is also available  
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## **News & Issues**

This issue covers regulatory and safety information on twenty drug (monocomponent and group) products. Also included are the recommendations from the WHO Consultation on Global Monitoring of Adverse Events Following Immunization (AEFI) held in Geneva 9-10 January 2006. This Consultation highlighted some important gaps in communication between groups monitoring adverse events following immunization (AEFIs) and groups recording adverse drug reactions (ADRs) at the country level. While both AEFI and ADR monitoring operations are less than optimal in most countries, any national surveillance system currently in place should be put to full use, to cover both AEFI and ADR functions. But whatever the measure, quality and comprehensive reporting will remain key factors in determining the practical use of pharmacovigilance.

WHO warns that while medicines are essential to alleviate suffering and are a core element in all international relief efforts, inappropriate donations may cause more harm than good. The WHO guidelines for appropriate drug donations should be consulted when contributing medicines for relief efforts. These guidelines can be accessed at:  
[http://www.euro.who.int/document/EHA/PAR\\_Donate\\_Guidelines.pdf](http://www.euro.who.int/document/EHA/PAR_Donate_Guidelines.pdf)

Two pharmacovigilance training courses will be offered in the month of September: one on pharmacovigilance for HIV/AIDS medicines in Barbados and the other in Botswana, on the general principles of pharmacovigilance. A report from these as well as relevant course materials will be made available on the WHO Medicines website in the near future.

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## ADHD Drugs Labelling revised

**Canada.** According to Health Canada, the prescribing information for all attention deficit hyperactivity disorder (ADHD) drugs has been revised in Canada to include standardized prescribing information that identifies risk factors for cardiac-related adverse events (AEs), and to provide recommendations to reduce these risks. This applies to the following drugs and all products containing these drugs: methylphenidate (e.g., Ritalin) and methylphenidate extended release (Ritalin SR), dexamethylphenidate (Attenade), dexamfetamine (Dexedrine), atomoxetine (Strattera). The revisions affect the Dosing recommendations, Contraindications, Warnings and Precautions, and Information for the Patient. Health professionals are advised that ADHD drugs should be started at the lowest dose and increased slowly, and should not be given to patients with a symptomatic heart disorder, advanced arteriosclerosis, hyperthyroidism, moderate to severe hypertension, or structural cardiac abnormalities; further cardiovascular (CV) system evaluation may be considered before starting ADHD drugs in patients with relevant risk factors, and patients who require long-term ADHD drugs should undergo periodic CV status evaluation. Patients are advised to not discontinue ADHD drugs without consulting their doctor, and to inform their doctor if they are using other ADHD drugs, are involved in strenuous activity, have certain heart disorders or a family history of sudden cardiac death, before using these drugs. Health Canada states that, theoretically, a pharmacological potential for all ADHD drugs to increase the risk of sudden cardiac death exists, but ADHD drugs are generally safe and beneficial when used as directed. (See WHO Pharmaceuticals Newsletter No. 2, 2006 for similar

directives in the UK following the conclusion of a Europe-wide review on the health risks and benefits of atomoxetine).

### Reference:

*Advisories, Warnings and Recalls. Health Canada, 26 May 2006*  
(<http://www.hc-sc.gc.ca>).

## *Cimicifuga racemosa* (Black Cohosh) Concerns of liver injury

**Europe.** The European Medicines Agency (EMA) and the Committee on Herbal Medicinal Products (HMPC) have become aware of case reports of hepatotoxicity in patients receiving *Cimicifuga racemosa* (Black Cohosh) root and, after reviewing available data, the HMPC considered that there is a potential association between hepatotoxicity and herbal medicines containing *Cimicifuga* (1).

Black Cohosh has been used traditionally for various purposes, including amenorrhoea and menopause symptoms. According to the EMA, 16 of the 42 case reports of hepatotoxicity evaluated by the HMPC were sufficiently documented to enable the HMPC to assess if *Cimicifuga* may be linked to the liver injuries and, as a result of the assessment, five cases were excluded, seven were thought to be unlikely related and there was a temporal association between the initiation of *Cimicifuga* treatment and the occurrence of the hepatic reaction in four cases. All new safety information related to this issue will continue to be reviewed by the HMPC, says the EMA.

The EMA advises patients to discontinue use of *Cimicifuga* and consult their doctor immediately if symptoms and signs suggestive of liver injury develop, and to inform their doctor if they are using herbal

medicine products. The EMA advises health-care professionals to ask patients about the use of *Cimicifuga*-containing products, and to report suspected hepatic reactions to the national adverse reaction reporting schemes. The United Kingdom's Medicines and Healthcare products Regulatory Agency (MHRA) says that warnings are to be added to the labels of *Cimicifuga* products, and that the Agency is working with the herbal sector to ensure the public is aware of the possible risk (2). Professor Kent Woods, MHRA Chief Executive, says that the labels of *Cimicifuga* products "will point out the possible symptoms so that appropriate action can be taken without delay".

(Reports in WHO database: *Cimicifuga racemosa*: Hepatic function abnormal - 14, Hepatic failure - 2, Gamma-GT increased - 3).

### References:

1. *Public Statement. European Medicines Agency, 18 July 2006*  
(<http://www.emea.eu.int>).
2. *Press Release. Medicines and Healthcare products Regulatory Agency (MHRA), 18 July 2006,*  
(<http://www.mhra.gov.uk>).

## Fluoxetine Use extended to include paediatric patients

**Europe.** The EMA has approved that the indication for fluoxetine (Prozac and associated products) can be extended to include the treatment of moderate to severe depression in children, eight years of age or older, who do not respond to psychological therapy. The Agency's Committee for Medicinal Products for Human Use (CHMP) concluded that the benefits of fluoxetine in this indication outweigh its potential risks. However, the Marketing Authorization Holder (Eli Lilly for Prozac) has been directed to