WHO PHARMACEUTICALS NEWSLETTER

World Health Organization

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 on our Internet website:
http://www.who.int/medicines

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No. 3, 2006

News & Issues

Last month the World Health Organization lost its Director-General, Dr Lee Jong-wook to a cerebral stroke. He was sixty one. Dr Lee became Director-General of the World Health Organization on 21 July 2003. Before that, he had worked for more than 20 years for the Organization, first battling leprosy in the South Pacific islands, then tackling vaccine preventable diseases including polio. During his all too brief tenure as Director-General, he pioneered new ways for people to gain access to tuberculosis and HIV/AIDS medicines, making this issue a serious political objective.

Dr Lee was a "man of action", whose adventurous spirit led him to "experience more, see more, and do more," said his son Tadahiro. We keep Dr Lee's family in our prayers.

Printed by the WHO Document Production Services, Geneva, Switzerland

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Safety of Medicines

Feature

Acetylcysteine
New paediatric dosing information

USA. The United States Food and Drug Administration (US FDA) has approved acetylcysteine (Acetadote) labelling updates, which included important new information for the treatment of paracetamol overdose in paediatric patients, according to Cumberland Pharmaceuticals. The updated labelling highlights new paediatric dosing information and includes a change in the loading dose duration from 15 to 60 minutes, says the company. AJ Kazimi from Cumberland Pharmaceuticals says that studies show that cases of paracetamol poisoning in the US are on the rise with up to 70% cases occurring in children less than 19 years of age.

Reference:

Media Release. Cumberland Pharmaceuticals Inc., 6 March 2006 (http://www.cumberlandpharma.com).

Anabolic steroids
Not to be sold as dietary supplements

USA, Canada. The US FDA has warned that the continued distribution and sale of certain unapproved drugs (Anabolic Xtreme Superdrol, Methyl-1-P) containing steroids without FDA approval could result in regulatory action against the concerned manufacturers and distributors (1). US FDA says that the products are not dietary supplements, as represented by the companies, because the active ingredients are not dietary ingredients. The products claim to be anabolic and are promoted for building muscle and increasing strength. The US FDA is concerned that consumers using these products may develop serious long-term health consequences associated with anabolic steroids including liver toxicity and testicular atrophy, gynaecomastia and infertility in men, (masculinization) in women, short stature in children, lipid metabolism disorders, increased risk of myocardial infarction and stroke. The US FDA advises consumers to stop taking these products, and to return the products to their place of purchase. Health Canada has issued an Advisory, warning consumers not to use five products (Anabolic Xtreme Superdrol, Methyl-1-P, Ergomax LMG, Prostanozoland, and FiniGenx Magnum Liquid) containing illegal anabolic steroids as they can potentially have serious health effects (2).

References:

1. FDA News. United States Food and Drug Administration, 9 March 2006 (http://www.fda.gov).
2. Advisory. Health Canada, 21 April 2006 (http://www.hc-sc.gc.ca).

Denileukin diftitox
Label to include reports of visual loss

USA. Ligand Pharmaceuticals Inc. has issued a `Dear Health-care Professional' letter to advise of changes to denileukin diftitox (Ontak) labelling with regard to visual loss. Denileukin diftitox is indicated for the treatment of patients with persistent or recurrent cutaneous T-cell lymphoma. Ligand says that the Warnings section has been updated to advise that loss of visual acuity, usually with loss of colour vision with or without retinal pigment mottling, has been reported following denileukin diftitox (Ontak) administration. Furthermore, recovery was reported in some patients, but most reported persistent visual impairment. According to the company, the Adverse Reactions section has also been updated, and says that because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to estimate their frequency reliably, or to establish a causal relationship to drug exposure.

Reference:

'Dear Health-care Professional' letter from Ligand Pharmaceuticals Inc., 3 March 2006 (http://www.fda.gov).

l-Arginine
Not for heart patients

Canada. According to Health Canada, patients who have previously had a heart attack should not use l-arginine supplements because of a recent study showing an increased potential risk of death when used after a heart attack (1). l-Arginine is an amino acid which is commonly used to sustain and promote healthy heart function. However a recent study published in the Journal of the American Medical Association in January 2006 suggests that l-arginine may not help improve heart and circulatory function following a first heart attack and may be associated with an increased risk of death when used after a heart attack (2). All l-arginine products are now required to carry a warning on their label reflecting this recent scientific information. Health Canada advises that for patients who have not had a previous heart attack, taking l-arginine is unlikely to present a risk and may provide benefits by helping the body repair damage to blood vessels in the heart.

Reference:

1. Advisory. Health Canada, 16 May 2006 (http://www.hc-sc.gc.ca).
2. Schulman SP et al. l-Arginine therapy in acute myocardial infarction. The Journal of the American Medical Association, 2006, 295: 58-64.

Pegaptanib sodium

Reports of anaphylaxis/anaphylactoid reactions

USA. The US Prescribing Information for pegaptanib injection (Macugen) has been amended following rare, US postmarketing reports of anaphylaxis/anaphylactoid reactions associated with intravitreal pegaptanib administration. Pegaptanib sodium injection (Macugen) is indicated for the treatment of neovascular (wet) age-related macular degeneration. The updated product label advises that pegaptanib (Macugen) is contraindicated in patients with known hypersensitivity to pegaptanib or other excipients in the product, and that a patient's medical history should be evaluated for hypersensitivity reactions prior to performing the intravitreal procedure; updates to the Precautions and Adverse Events sections have also been made to highlight the reports of anaphylaxis/anaphylactoid reactions. The companies (OSI) Eyetech Inc. and Pfizer Inc. say that a direct link between pegaptanib or the various medications, and the anaphylaxis/anaphylactoid cases, which include angioedema, has not been established (see WHO Pharmaceuticals Newsletter No. 2, 2006 for Health Canada - endorsed safety information on pegaptanib).

Reference:

'Dear Health-care Professional' letter from (OSI) Eyetech Inc. and Pfizer Inc., 6 March 2006 (http://www.fda.gov).

Bowel cleansing oral sodium phosphates

Risk of renal damage

USA. The US FDA has issued an alert that acute phosphate nephropathy, a type of acute renal failure, is a rare but serious adverse event associated with the use of oral sodium phosphates (OSP) for bowel cleansing. According to the Alert, acute phosphate nephropathy has been documented in 21 patients who used an OSP solution and in one patient who used an OSP tablet; older individuals, those with kidney disease or decreased intravascular volume, and those using medicines that affect renal perfusion or function (diuretics, angiotensin converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARBs), and possibly nonsteroidal anti-inflammatory drugs) are at higher risk of acute phosphate nephropathy.

Reference:
FDA Alert. United States Food and Drug Administration, May 2006 (http://www.fda.gov).

Glucosamine products

86 reports to date in Sweden

Artrox, Glucosine, Glukosamin Copyfarm and Glukosamin Pharma. According to the Agency, previously unknown adverse reactions of particular interest included the following: angioedema (n = 2), urticaria (1), colitis (2), gastric/duodenal ulcer (3), oedema/lower limb oedema (3), dizziness (4), arthralgia (2), bronchial asthma/bronchial asthma aggravated (3), diabetes aggravated (2) and hypercholesterolaemia (2). There were also three cases of an increased effect of warfarin during concomitant treatment with glucosamine products.

(Reports in WHO database: All reactions - 645).

Reference:
Three year adverse reaction follow-up of glucosamine products as drugs. Swedish Medical Products Agency, 21 April 2006 (http://www.moa.se).

Isotretinoin

Suspected association with vascular disorders

Canada. Health Canada has received 29 domestic reports of suspected isotretinoin (Accutane)-associated vascular disorders between the time the drug was marketed in Canada (1983) and 31 December 2005, according to an article in the *Canadian Adverse Reaction*

unknown for the remaining two patients.

(Reports in WHO database: Vascular disorder - 26).

Reference:
Canadian Adverse Reaction Newsletter, April 2006, 16(2): 3.

Mifepristone

Two additional sepsis deaths

USA. Danco Laboratories has informed the US FDA of two additional deaths following medical abortion with mifepristone (Mifeprex), according to an US FDA Public Health Advisory; the US FDA is investigating all circumstances surrounding the cases, and cannot confirm the causes of death. Four previous deaths from sepsis associated with off-label mifepristone (Mifeprex) and misoprostol use have been reported to the US FDA. The US FDA advises that all medical abortion providers and their patients should be aware of risks associated with mifepristone use, including sepsis, and that physicians should discuss early potential signs and symptoms warranting immediate medical evaluation. The FDA reiterates the approved mifepristone (Mifeprex) regimen for medical abortion, including misoprostol use; the US FDA says that these recommendations are