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REGULATORY NEWS

- **Efalizumab (Raptiva) removed from the market in Canada and the EU:** The European Medicines Agency conducted a risk/benefit analysis and recommended on February 19th that efalizumab should be removed from the market in Europe because the risks outweigh the benefits. The main concern arose when cases of progressive multifocal leukoencephalopathy (PML), including 2 deaths, as well as reports of Guillain-Barre syndrome, encephalitis, and meningitis were reported in patients taking efalizumab. PML is a potential fatal demyelinating disease of the CNS caused by reactivation of the JC virus. The manufacturer stopped selling this drug in Canada the next day. The FDA issued a public health advisory but to date the drug has not been removed from the market in the US.[1-4]
- **Observe patients taking natalizumab for symptoms of PML:** PML has rarely been reported in patients taking natalizumab. Symptoms include weakness, clumsiness, vision disturbances, and changes in cognition.[4]
- **Important changes in dose conversion guidelines for fentanyl transdermal:** Two analgesic equivalency tables are provided on the Health Canada website[5] for safe conversion to fentanyl transdermal systems.
- **Topical anesthetic warnings:** Health Canada issued a warning concerning topical anesthetic products such as Emla and compounded products. Excessive exposure has lead to methemoglobinemia, CNS toxicity and cardiovascular collapse, especially if large amounts are applied prior to laser hair removal. Application to damaged skin or under occlusion can increase drug absorption and toxicity.[6] The FDA issued a safety warning following the publication of a study on the use of 4% topical lidocaine gel to reduce discomfort during mammographic procedures. In this small study, no adverse events were seen, but the concern is that large amounts of lidocaine could be absorbed, especially with plastic wrapping, leading to lidocaine toxicity.[7,8]

- **More adulterated drugs discovered:** Health Canada and the FDA issued warnings on 68 “natural” products promoted for weight loss that were found to contain undeclared sibutramine, phenytoin, bumetanide, rimonabant, and/or phenolphthalein. [9,10]
- **Movie-goers in the UK view dead rat warning about the risk of fake drugs purchased over the internet:** In the UK, 33,000 men buy drugs over the internet, and it is estimated that 50-90% of these drugs are counterfeit. To warn of the dangers of buying drugs from unregulated sources, a unique advertisement has been shown in UK cinemas since January 19th. The advertisement shows a man coughing up a dead rat after ingesting a pill bought on the internet. It can be viewed at www.realdanger.co.uk (warning: it is quite graphic).[11]

CLINICAL STUDIES AND CASES

- **Hospital discharge improvements by nurses and pharmacists:** Adverse events are common after patients are discharged from hospital. This study used a nurse discharge advocate plus a clinical pharmacist to coordinate discharges. The discharge plan was done by the nurse. The clinical pharmacist telephoned the patient a few days after discharge to review medication use. Fifty-three percent of patients needed help from the pharmacists, such as contacting the prescriber. The interventions decreased post-discharge hospital visits by about 30%.[12]
- **Text messaging to deliver pharmaceutical care:** In this pilot study, patients were texted reminders about their medication. For example, a text message would be sent ten minutes before the time when the medication should be taken, and a reminder was sent to renew the prescription at the time of the last dose. The patients were also sent lists of the most common adverse reactions that might occur, with a reminder to contact a pharmacist if an ADR occurred. Despite these reminders, many patients did not take their medications on time. However, many patients appreciated the messages about precautions.[13]
- **Bisphosphonate adverse effects:** A number of uncommon ADRs have now been identified for bisphosphonates: femoral fractures, osteonecrosis of the jaw, and severe musculoskeletal pain. It is unclear if these drugs increase the risk of esophageal cancer; cases have been reported but causality is uncertain.[14]
- **Rare Gardasil® reactions:** In Australia there have been five reports of CNS demyelination 1-21 days after a 2nd or 3rd vaccination with Gardasil®. Three of the women had a history of neurological episodes and were subsequently diagnosed with multiple sclerosis (MS). The women developed partial transverse myelitis (inflammation of the spinal cord), hemiparesis (muscle weakness on one side of the body), or limb pseudoathetosis (abnormal writhing movements, usually of the fingers; see video at http://www.asktheneurologist.com/movement-disorders-lecture.html). All five women had partial or complete recovery. The authors conclude that, while MS is more common in young women, the atypical presentations and timing suggest that Gardasil® may influence CNS inflammation. Caution may be warranted in patients with MS.[15] Six adolescent girls developed stroke, DVT or pulmonary embolism after immunization with HPV vaccine. A causal relationship is unclear, since the girls had other factors that might have been contributory such as treatment with oral contraceptives. [16]
- **Possible interaction between clopidogrel and PPIs:** Controversy exists over whether or not PPIs reduce the clinical benefits of clopidogrel. In this new study, all-cause mortality or rehospitalisation for acute coronary syndromes was significantly increased (adjusted OR 1.25) in patients who took a PPI (60% took omeprazole) along with clopidogrel. Clopidogrel is a prodrug that requires activation by a variety of P450

enzymes including CYP2C19, and PPIs inhibit CYP2C19 in vitro. Further research is needed to determine the clinical impact of this interaction and which PPIs interact.[17,18]

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We are grateful to all the First Nations who have cared for and nurtured the lands and waters around us for all time, including the x?m??k??y??m (Musqueam), Sk?wx?wu?7mesh U?xwumixw (Squamish Nation), and s?l?ílw?ta? (Tsleil-Waututh Nation) on whose unceded and ancestral territory our centre is located.

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