re:Action No. 39

June 2010 **yccwm.org.uk**

A quarterly bulletin from the Yellow Card Centre West Midlands

Welcome to our new-look quarterly bulletin

The Yellow Card Centre West Midlands exists to promote the reporting of adverse drug reactions and raise general awareness of iatrogenic disease. If you would like to receive this bulletin by email contact: help@yccwm.org.uk

CK & you shall find

Drug Safety Update 2010;**3(10)**:7–8

HMG-CoA reductase inhibitors (statins) are widely prescribed and effective drugs, used for the reduction of low-density lipoprotein cholesterol. Although they have a positive safety profile, muscle-related adverse effects are common. Symptoms range from mild myopathies and myalgias, to myositis, to rare cases of potentially life-threatening rhabdomyolysis.

The MHRA have warned of an increase in the risk of myopathy with high-dose (80 mg) simvastatin. This warning followed an analysis of the Study of the Effectiveness of Additional Reductions in Cholesterol and Homocysteine (SEARCH) which compared a 80 mg dose of simvastatin with 20 mg simvastatin. Treatment with simvastatin 80 mg did not show any significant benefits over simvastatin 20 mg in reducing major cardiovascular events, but myopathy and rhabdomyolysis were more common (Table 1).

Table 1: Incidence of myopathy & rhabdomyolysis in the SEARCH study.

Simvastatin 20mg (n=6033)	Simvastatin 80mg (n=6031)
Myopathy	
0.02% (n=1)	0.9% (n=52)
Rhabdomyolysis	
0% (n=0)	0.2% (n=11)

Chatzizisis et al (*Drug Safety* 2010;**33(3)**:171–187) recently reviewed the factors that increase the risk of statin-related myopathy. Higher doses of statins were associated with an increased risk of myopathy, although there was no reliable comparative data for different statins. Patient factors they found are summarized in Table 2.

Co-morbidities include renal impairment, hypothyroidism, high alcohol consumption, a previous history of statin related muscle problems, and a family history of muscle problems are at higher risk.

Table 2: Risk factors for statin-induced myopathy

Patient characteristics	Concomitant medications
Increased age Race Female Gender Co-enzyme Q10 depletion Genetic predisposition Co-morbidities	Cytochrome P450 interactions Glucuronidation interactions

The MHRA has issued the following advice:

- Simvastatin 80 mg should only be considered in patients with severe hypercholesterolaemia and high-risk of cardiovascular complications who have not achieved their treatment goals on lower doses, and when the benefits are expected to outweigh the potential risks
- Patients already taking 80 mg may need review in the light of this new evidence
- Patients currently taking 80 mg of simvastatin should not stop treatment, but should contact their doctor immediately if they have unexplained muscle pain, tenderness or weakness

A recent paper in the BMJ (*BMJ* 2010;**340**:c2197) found the number needed to harm (NNH) for moderate to severe myopathy was 259 (women) and 91 (men) for patients taking any statins who were considered to be at cardiovascular risk.

We welcome reports of suspected muscle pains to statins via the Yellow Card scheme.

Gd can be bad

The European Medicines Agency's Committee for Medicinal Products for Human Use (CHMP) recently reviewed MRI contrast agents, which are chelates of gadolinium. The CHMP has recommended restrictions on their use.

The review arose following concerns about nephrogenic systemic fibrosis (NSF) in 2006. NSF is a rare disease first described in 2006, which causes thickening of the skin and connective tissue in those with severe renal disease.

It is likely to result from free gadolinium, and so from less stable linear chelates. Gadolinium-containing products are characterised as low, medium, and high risk for NSF. The CHMP have made a number of recommendations that include restricting or issuing cautions about their use in those with kidney disease, infants, those breastfeeding, and the elderly.

Those using gadolinium-containing contrast agents should read the EMEA guidance available at http://emea.europa.eu We welcome any reports of suspected reactions to contrast media.

Drugs under intensive surveillance

Drugs indicated by a black triangle within the BNF are subject to intensive surveillance. Any reaction, no matter how trivial, should be reported. The following are recent additions to the intensive surveillance scheme.

Dronedarone (Multaq®)	Atrial fibrillation
Amifampridine (Firdapse®)	Lambert-Eaton Myasthenic Syndrome (LEMS)

Asleep at the wheel

Am J Forensic Psychaitr 2010;3**1(1)**:5–15

An American woman took 10 mg of zolpidem and quetiapine, with several glasses of wine and went to bed. She was found later in the evening by the Police driving erratically at slow speed with her hazard lights on. Her behaviour was described as "out of it", and she closed her eyes when speaking to the police. She was convicted of drink-driving in 2006, but had no memory of the incident.

In 2007, the US FDA issued warnings of sleep-driving associated with zolpidem, and her conviction was quashed on appeal.

Zolpidem has been associated with a number of noctural activities with associated amnesia, including sleep-driving, nocturnal eating, and unconscious sexual activity while asleep. The use of alcohol or other psychoactive drugs appears to increase the risk of such reactions. (*Aust Prescr* 2008;**31**:146-9) The Australian Adverse Drug Reactions Advisory Committee (ADRAC) has also reported sleep walking and strange automated behaviour while asleep, such as binge eating and house painting. In the UK, the MHRA Yellow Card database lists 8 reactions of amnesia, and 6 cases of somnambulism.

We would welcome any reports of unusual sleep disturbance related to prescribed medication. Patients and healthcare professionals can report suspected adverse reactions at http://www.mhra.gov.uk/yellowcard

ADR training

If you require a speaker for a lunchtime meeting or your educational programme, why not contact our unit?

Our centre is keen to promote the Yellow Card scheme, and can provide training on adverse drug reactions and pharmacovigilance. We will visit any location in the West Midlands region.

Call 0121 507 5672 or email help@yccwm.org.uk now to arrange a booking.

Yellow Card Centre West Midlands

We encourage Yellow Card reports for all suspected adverse drug reactions to new (▼) drugs, vaccines and unlicenced herbal remedies, all suspected reactions in children, and serious or unusual reactions to well-established drugs. You do not have to be certain a drug caused a reaction to report it.

Please send report to MHRA, CHM, Freepost, London, SW1W 9SZ or use www.mhra.gov.uk/yellowcard

Comments about this bulletin can be sent to Prof R.E. Ferner at r.e.ferner@bham.ac.uk