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An occasional bulletin from the West Midlands Centre for Adverse Drug Reaction Reporting

Celebrating forty years of the Yellow Card Scheme

Please let us know if you would like to receive this bulletin by email: help@csmwm.org

Forty years of pharmacovigilance

This year the Yellow Card Scheme will be forty years old. As the scheme approaches middle age, its value as a method of discovering important drug safety signals remains immense.

The Yellow Card scheme was set up in the wake of the thalidomide tragedy, which left behind 10,000 children with congenital deformities. The scheme was designed to discover quickly adverse effects, that otherwise might take years to discover through the tortuous process of publication of cases in the medical literature.

The Chairman of the Committee on Safety of Drugs (now called the Committee on the Safety of Medicines), Derrick Dunlop, laid out four core principles about the Yellow Card Scheme when he announced the scheme:

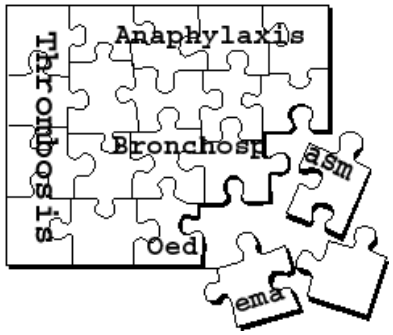
1. Suspected reactions should be reported; reporters do not need to be certain or to prove that the drug caused the reaction.
2. It is the responsibility of all doctors and dentists to report.
3. Reporters should report without delay.
4. Reports could be made and would be treated in confidence.

More recently, the scheme has been extended to pharmacists and nurses. Changes to the Yellow Card have been made to ensure the anonymity of patients. However, the scheme continues to operate on the four founding principles. Importantly, reports by healthcare professionals remain confidential.

The scheme still requires your help to maintain its important role in maintaining public health. Those who submit Yellow Card reports help to ensure that drugs are used safely, and so benefit the public's health.

Do my reports matter?

Finding the safety profile of a drug is similar to completing a large jigsaw without a final idea of its whole. By reporting an adverse drug reaction to us, you help to put a piece of that jigsaw in place. Without reporters to the scheme, the jigsaw would never be completed.



What has the Yellow Card Scheme achieved?

The Yellow Card scheme has provided valuable information about the safety of drugs, leading to improved prescribing advice, changes in manufacturers' licences, and drug withdrawals.

Table 1: A selection of recent early warnings from the Yellow Card Scheme.

1995 Tramadol	Psychiatric reactions	Warnings.
1995 quinolones	tendinitis	improved warnings.
1996 alendronic acid(Fosomax▼)	severe oesophageal damage	warnings and revised dosing instructions .
1999 A*ristolochia* in herbal remedies	renal failure	*Aristolochia* banned.
2001 bupropion (Zyban▼)	seizures	strengthened warnings and revised dosing instructions
2003 warfarin and cranberry juice	changes in INR	information provided in publications

Risk factors for myopathy and rhabdomyolysis with the statins (*ADRAC* 2004;**23(1)**:2)

An analysis of Australian spontaneous reports of rhabdomyolysis associated with statins has attempted to examine possible risk factors.

Table 2: Factors increasing the risk of muscle disorders with simvastatin and atorvastatin.

Substances inhibiting metabolism by CYP3A4	Ciclosporin, verapamil, macrolide antibiotics, diltiazem, -azole antifungals, protease inhibitors, grapefruit juice,
Concomitant lipid-lowering therapy	gemfibrozil and other fibrates
Disease states	diabetes, hypothyroidism, renal, high alcohol intake, and hepatic disease
Advanced age	≥ 70 years
High statin dose	≥ 40 mg/day

Other statins (fluvastatin, pravastatin and rosuvastatin) are not metabolized by CYP3A4 but are subject to other drug interactions.

CSM West Midlands has received 8 reports of rhabdomyolysis associated with statins. We would welcome any reports of serious adverse reactions to statins. Rosuvastatin (Crestor®) is a black triangle (▼) drug and we welcome any reports of suspected adverse reactions.

Bupropion and joints (*Joint Bone Spine.* 2004; In press)

Ornetti and colleagues report 4 cases of joint symptoms associated with bupropion (Zyban®), reported to a French Regional monitoring centre in the Bourgogne region.

All four patients had symptoms severe enough to require admission; three also had serum-sickness-like reactions. Time of onset varied from 5 to 15 days. Symptoms such as joint pain and urticaria started abruptly and ceased within a few days of discontinuing bupropion treatment.

The manufacturer warns that arthralgia, myalgia and fever in association with rash (suggestive of a delayed hypersensitivity-like serum sickness) are rare reactions occurring with a frequency of between 1 in 1000 and 1 in 10,000.

CSM West Midlands has received 11 reports of joint pain and arthralgia associated with bupropion, five of which were associated with urticaria or skin rashes.

Bupropion is a black triangle (▼) drug and we welcome any reports of suspected adverse reactions.

REPORTING TO CSM West Midlands

We welcome Yellow Card reports on all suspected adverse reactions to new (▼) drugs including vaccines and unlicensed herbal remedies and *all suspected reactions to all drugs used in children*, and on all serious or unusual reactions to well-established drugs. You do not have to be certain that a drug caused a reaction in order to report.

You can **download a copy of the redesigned yellow card in Adobe PDF format** from our website (http://csmwm.org).

Please send reports to: CSM West Midlands, Freepost SW2991, BIRMINGHAM, B18 7BR.
No stamp is needed. If you would like a supply of pre-addressed and reply-paid yellow cards, please contact the above address.

SOME ADDITIONS TO THE LIST OF INTENSIVELY MONITORED DRUGS

Approved name	Trade name	Indication
atanazavir	▼ Reyataz®	HIV-1 infected adults
bortezomib	▼ Velcade®	relapsed and refractory multiple myeloma
emtricitabine	▼ Emtriva®	HIV-1 infected adults and children
enfuvirtide	▼ Fuzeon ®	HIV-1 infected patients
porfimer sodium	▼ PhotoBarr®	high grade dysplasia in patients with Barrett's oesophagus

The entire list of about 220 intensively monitored drugs can be obtained from the centre or on our website: http://csmwm.org. Please report **all** adverse reactions you suspect are due to intensively monitored drugs. Please send any comments to: Dr R E Ferner at CSM West Midlands, or email: r.e.ferner@bham.ac.uk