



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

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

### Same old drugs, same old problems

(*BMJ* 2004; 329: 15-19)

A widely reported study on adverse drug reactions as a cause of hospital admissions has recently been published in the *BMJ*. In 18,820 admissions to hospital, 1225 admissions were related to an adverse drug reaction (6.5%). The authors estimated that the rate of death in UK hospitals, including those reactions occurring to patients after they had entered hospital, would be 10,000 a year. Well-established drugs figured prominently (**Figure 1**).

**Figure 1:** Drugs associated with ADRs

Drug/drug class	% of cases	Examples of major ADRs noted
NSAIDs	30%	bleeding, rash, CVA
diuretics	27%	renal impairment, hypotension, electrolyte disturbances, gout
warfarin	11%	bleeding
ACE inhibitors/AII receptor antagonists	8%	renal impairment, hypotension, electrolyte disturbances, angioedema
antidepressants	7%	confusion, hypotension, hyponatraemia
beta-blockers	7%	bradycardia, wheezing
opiates	6%	urinary retention, confusion, vomiting
digoxin	3%	digoxin toxicity
prednisolone	3%	GI bleeding, hyperglycaemia, osteoporotic fracture
clopidogrel	2%	GI bleeding

The authors correctly point out that because of a lack of knowledge about consumption data for all the drugs, that the appearance of a drug in the top ten may indicate that the drug is widely prescribed, rather than intrinsically more dangerous than other drugs. However, the absolute burden of these drugs is significant. Given that 70% may be possibly or definitely preventable, the next challenge is to develop mechanisms to prevent ADRs.

Some key issues in prescribing include:

1. Using a drug at the lowest dose necessary for benefit.
2. Ensuring that the benefits of the drug are likely to outweigh the risks.
3. Ensuring preventive treatments are prescribed appropriately (e.g. proton pump inhibitors or misoprostol in patients at risk of GI haemorrhage).
4. Giving clear advice to patients so they can respond appropriately to worrying symptoms.
5. Reviewing repeat prescriptions to check that the benefit of continuing still outweighs the risk of harms.

We welcome any reports of **any** suspected adverse drug reactions to well-established drugs causing hospitalization or serious reactions.

### Summer sun: focus on photosensitivity

The UK summer can be disappointing. However, a significant number of patients go on holiday to sunnier destinations, and sunny days at home can catch us unaware.

Doses of ultraviolet or visible light that would not usually cause sunburn can cause photosensitivity in the presence of some drugs. Many of the drugs commonly associated with photosensitivity reactions are widely prescribed. (**Figure 2**)

**Figure 2:** Drugs commonly associated with photosensitivity reactions (*Davies's Textbook of Adverse Drug Reactions*, 5<sup>th</sup> ed. 1998)

amiodarone thiazide diuretics non-steroidal anti-inflammatory drugs phenothiazines (e.g. chlorpromazine) sulphonamides tetracyclines isotretinoin
---

Specific advice for patients may be warranted to avoid photosensitivity, for example patients taking

amiodarone are advised to shield the skin from light and to use a wide-spectrum sunscreen.

The West Midlands Centre for Adverse Drug Reactions has received 99 reports of photosensitivity. The most common classes of drug involved included antidepressants (10 reports), diuretics (7), proton pump inhibitors (6) and NSAIDs (6).

We welcome reports of any suspected photosensitivity reactions.

### **Pancreatic toxic effects with combination antiretrovirals**

(*Lancet* 2004; **364**: 65-7)

A recent paper highlights the possible increase in risk of pancreatitis when didanosine and tenofovir are used in combination. Patients receiving didanosine and tenofovir (n=185) were compared with those taking tenofovir without didanosine (n=208) and those taking didanosine without tenofovir (n=182). Co-administration of both drugs was an independent risk factor for pancreatitis (crude hazard ratio 10.7, 95% CI 1.2-92, P=0.03) compared with either agent alone.

The West Midlands Centre for adverse Drug Reaction Reporting has received 2 reports of adverse pancreatic reactions to didanosine. We have not received any reactions associated with tenofovir. We would welcome any reports of interactions or adverse

reactions to these agents, as antiretrovirals are a particularly under-reported class of medicines.

### **Statins and thiazolidinediones**

(*Am J Cardiol* 2004; **93**: 1417-8)

Spontaneous reports of muscle, liver, pancreas and bone marrow adverse reactions to atorvastatin were 3 times more likely (95% CI 1.8–5.4, P<0.0001) to list concomitant treatment with rosiglitazone or pioglitazone than simvastatin. Most ADRs involved the muscles or liver. The authors acknowledged some limitations of their study (such as inability to control for confounders and reliance on FDA spontaneous reporting rates which may be prone to biases). They accept that it does not provide proof but is suggestive of an interaction between atorvastatin and thiazolidinediones, when using patients treated with simvastatin as a control group.

The increasing use of thiazolidinediones and aggressive use of statins may mean that such a combination will become increasingly common. While the potential for, and possible mechanism of, this potential interaction is still unknown, it is worth noting the increased likelihood of thiazolidinediones being listed as concomitant medicine with atorvastatin reactions compared to simvastatin.

We would welcome any reports of suspected interactions between thiazolidinediones and statins.

## **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. Advice on reporting is available at 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 us.

## **SOME ADDITIONS TO THE LIST OF INTENSIVELY MONITORED DRUGS**

Approved name	Trade name	Indication
modafinil	▼ Provigil®	excessive sleepiness associated with chronic pathological conditions
cetuximab	▼ Cetuximab®	growth factor receptor-expressing metastatic colorectal cancer
insulin detemir	▼ Levemir®	treatment of diabetes mellitus
epirubicin	▼ Pharmorubicin ®	antineoplastic agent
estradiol	▼ Naemis®	hormone replacement therapy

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](mailto:r.e.ferner@bham.ac.uk)