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

This bulletin and other items of news about the Centre are available on the internet at http://www.chtpharm.demon.co.uk/csmwm.htm

REPORTING TO CSM West Midlands

We welcome Yellow Card reports on all adverse reactions to new (−) drugs including vaccines and unlicensed herbal remedies, and on all serious or unusual reactions to well-established drugs.

Yellow Cards can be found in the BNF, MIMS, the ABPI Compendium of Data Sheets, OTC Directory and in FP10 prescription pads. Further supplies can be obtained from CSM West Midlands.

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.

ADDITIONS TO CLOSELY MONITORED DRUGS include

Approved name	Trade name	Indication
−alprostadil	MUSE®	erectile dysfunction
−cefprozil	Cefzil®	mild to moderate infections: URTIs, otitis media and skin infections
−grepafloxacin	Raxar®	community acquired pneumonia, chronic bronchitis exacerbation, and *Chlamydia trachomatis* infections
−lercanidipine	Zanidip®	hypertension
−modafinil	Provigil®	narcolepsy
−montelukast	Singulair®	prophylaxis of asthma
−rivastigmine	Exelon®	mild to moderate Alzheimer's disease
−tolterodine	Detrusitol®	bladder instability

There are around 170 drugs on the closely monitored list. An up-to-date list can be obtained from the centre or on our internet site. Please report <u>all</u> adverse reactions you suspect are due to closely monitored drugs.

RECENT REPORTS

Getting to the heart of diabetes... Calcium antagonists (N. Eng. J. Med. 1998; 338: 645-52, Circulation 1997; 96(suppl. 1): I-764, Lancet 1998; 351: 1755-62)

Recently there have been two randomized controlled studies published in which there was a striking difference in cardiovascular events between non-insulin dependent diabetics who were taking a calcium antagonist and those who were taking an ACE-inhibitor. This follows earlier case-control studies that suggested that high doses of short-acting, but not long-acting, dihydropyridine calcium antagonists were associated with an excess risk of cardiac events. This supports the biologically plausible hypothesis that diabetic patients have an increased susceptibility to the adverse effects of calcium antagonists.
The most recent study (the HOT randomised trial) points to a slightly different explanation: ACE-Is are especially beneficial in patients with diabetes mellitus.

We welcome reports of serious reactions to established drugs, even if the reaction is well documented as it may

provide information on vulnerable patient populations. Any reaction which results in hospital admission is sufficiently serious to merit reporting.

Keep taking the medicine?... SSRIs and withdrawal reactions (Eur. J. Clin. Pharmacol. 1997; 53: 163-9)

A recent investigation of almost 50 000 cases of adverse reactions to SSRIs reported to the WHO database from 16 countries suggests that the reporting rate of withdrawal reactions to SSRIs is considerably higher with paroxetine than with sertraline or fluoxetine.

Withdrawal symptoms related to the central nervous system - dizziness, headache, seizures, paraesthesiae, vertigo, for example - were predominately associated with paroxetine and sertraline. Fluoxetine, however, was predominately associated with psychiatric symptoms, for example, nervousness, anxiety, suicide attempt, aggression and agitation.

We receive several reports of reactions to SSRIs each month, some of which are withdrawal reactions. We welcome reports of serious reactions to these drugs. In cases of withdrawal reactions, information should be given on the nature and timing of the drug withdrawal, details of any treatment required to treat the reaction and the eventual outcome.

GI reactions to NSAIDs (Bandolier 1998; 52: 2-6)

In the last three months we have received six reports of GI problems related to NSAID use. Of these, five resulted in hospital admission. A recent review in Bandolier has shown that these six reports are likely to have been only a very small fraction of NSAID-associated GI reactions which have occurred.

Perhaps 1-3% of users of NSAIDs develop overt GI bleeding and 26% will be prescribed anti-ulcer therapy. There are estimated to be 3,500-12,000 NSAID-related admissions in the UK each year. GI bleeding, and any other reaction which results in hospital admission, is a serious reaction and should be reported even for drugs such as NSAIDs where this problem is well-known. The Yellow Card scheme is also used to identify risk factors as well as identify previously unknown reactions.

We welcome reports of GI bleeding associated with NSAID use and all other serious reactions even if they are well-known.

The problems of interactions - the withdrawal of mibefradil

Mibefradil has been recently withdrawn voluntarily. As more and more potential drug interactions were recognized it became increasingly difficult for patients to comply with the complexity of the labelling instructions. Mibefradil inhibits the isoenzymes of the cytochrome P450 enzyme system and co-administration with other drugs metabolized by these isoenzymes may lead to increased plasma concentration of these drugs. We received eight reports of reactions associated with the use of mibefradil. In four of these cases, there was concurrent administration of another drug metabolised by the P450 system. Drugs which are metabolised by the P450 system include terfenadine, astemizole, cisapride, digoxin, cyclosporin, and certain statins, beta-blockers and ACE-inhibitors.

We welcome reports of suspected drug interactions particularly when the interaction is not documented. Any interaction which results in a serious reaction should be reported.

Please send any comments, questions or suggestions to:

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