re:ACTION January 2001 No.21

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

This bulletin (complete with an index of all past issues) and other items of news about the Centre are available on the internet at **http://csmwm.org**

If you would like to receive this bulletin by email, please let us know: help@csmwm.org

RECENT REPORTS

The Black triangle (–) - what does it mean?

An inverted black triangle **(–)** next to a product in the British National Formulary, MIMS, Data Sheet Compendium and Summary of Product Characteristics indicates that the Medicines Control Agency is intensively monitoring that product. In general, all new drugs are assigned a black triangle for a period of approximately two years after licensing. During this time the MCA ask for all suspected reactions, however minor they seem, to be reported. Drugs, before licensing, are tested in relatively few patients and some quite common adverse effects may not have been detected in the clinical trials [see How safe is safe? re:Action No8, 1995].

After the end of this two year period a safety review of all the available data, not just yellow cards, is carried out and if there are still any safety concerns the black triangle will remain until further review.

Black triangles are also used to designate some well-established drugs used in new indications, or in a new combination or formulation. Cozaar-Comp® (losartan and hydrochlorothiazide) and Ventolin Evohaler® (salbutamol) are examples. An up-to-date list can be found on our website.

Keeping an eye on interactions: warfarin and celecoxib (Southern Med. J. 2000; 93: 930-2)

A recent case report recounts a 71-year old man who had been on a complex drug regimen which included warfarin and cimetidine. The INR had been between 1.9 - 2.9 for 6 months with no changes of warfarin dose in this period Seven days after beginning treatment with celecoxib the patient presented with melaena and the INR had risen to 4.0. Endoscopy revealed an ulcer and diffuse haemorrhagic gastropathy.

The authors suggest that the celecoxib may have affected the metabolism of warfarin or cimetidine or both, and that the celecoxib was responsible for the gastropathy.

At CSM West Midlands, we have had a total of 19 reports of reactions to celecoxib since it was licensed earlier this year. In one case a 79-year old man experienced melaena 14 days after starting celecoxib 400mg. None of these cases involved concomitant warfarin and celecoxib use.

We welcome any reports of suspected reactions to or interactions with celecoxib and rofecoxib

Warfarin – still a bleeding nuisance
(European Society of Pharmacovigilance, 2000)

A recent study by CSM West Midlands in a Birmingham teaching hospital found warfarin to be the most common reason for drug induced admissions to hospital over a three month period. A quarter of the patients whose admission was precipitated by drugs had haemorrhage from warfarin.

At CSM West Midlands we have received 3 reports of haemorrhage due to warfarin over the past year, all of which were serious. Some reports were associated with known interactions with co-prescribed medication.

Patients taking warfarin should be warned about the potential for bleeding with warfarin especially when

other drugs are given in addition, and the importance of seeking medical advice in the event of unusual bleeding or bruising.

The CSM welcomes reports of serious reactions to, or interactions with, well known drugs, even if such reactions are well documented.

Aspirin, double edged sword? (BMJ 2000; 321: 1183-7)

A recent meta-analysis looking at 24 trials involving 66,000 patients found that 2.47% of patients taking aspirin suffered gastrointestinal haemorrhage compared to 1.42% taking placebo. About 1 in 100 patients taking aspirin over a 28 month period will experience a gastrointestinal haemorrhage. Slow release preparations were not shown to reduce the haemorrhage rate and no significant reduction in rates of gastrointestinal haemorrhage were found.

We have received 6 reports of GI haemorrhage with aspirin in the past year. Five of the patients were aged 60 years or older and all were taking 75 mg per day.

Gastrointestinal haemorrhage is a serious reaction and the CSM welcomes reports of well known serious reactions to established drugs. Such reports allow the CSM to monitor the safety of such agents and discover factors increasing the risk of such reactions.

Assessing serious reactions (J. Clin. Pharm. Therapeut. 2000; 25: 355-61)

All reactions which result in the admission of the patient to hospital are defined by the MCA as serious. All such reactions can be reported via the Yellow Card scheme, but few are.

A recent pilot study conducted in an acute medical assessment unit in a Liverpool teaching hospital found that an adverse drug reaction was responsible for 15 (7.5%) of 200 randomly selected admissions. Two of the 15 patients subsequently died. None of these reactions were reported as ADRs using the Trust's in-house reporting scheme. The drugs implicated most often were NSAIDs and drug used to treat cardiovascular disorders.

We welcome reports from GPs as well as admitting doctors of all reactions which result in hospital admission. We take care to identify duplicate reports, so you should not be deterred from reporting by concerns that a reaction will be reported more than once.

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.

Since the issue of the GMC's guidelines on patient confidentiality we no longer require the patient's name or date of birth. However, you should given sufficient details to enable **you** to identify the patient if we should need to contact you about the reaction. You can now **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.

ADDITIONS TO THE LIST OF INTENSIVELY MONITORED – DRUGS

Approved name	Trade name	Indication
esomeprazole	– Nexium®	GORD and eradication of *H. pylori*
galantamine	– Reminyl®	mild to moderate Alzheimer's disease
levetiracetam	– Keppra®	adjunct therapy in epilepsy
pioglitazone	– Actos®	oral treatment of type II diabetes
trastuzumab	– Herceptin®	advanced breast cancer
tropsium chloride	– Regurin®	urinary frequency

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