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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

Bee careful

(*Canadian Adverse Reaction Newsletter* 2005; **15(2)**: 2-3)

Apitherapy, the medical use of honeybee products, is gaining in popularity. Medicinal claims made for honeybee products include anti-fungal and anti-bacterial activity, immune system stimulation, and a variety of other conditions from asthma to impotence.

Health Canada has received fourteen reports of suspected adverse reactions associated with bee products, including as bee pollen, royal jelly and propolis, in the past 6 years. Ten of the reactions were considered serious. Some reports were allergic in nature: acute oral and laryngotracheal oedema with respiratory distress; suspected autoimmune hepatitis; oedema, rash and urticaria; and a possible allergic reaction with chest pain. Other serious reactions were bleeding, hepatitis and seizures.

It is not possible to be sure that the bee products caused the adverse effects, because of confounding factors such as pre-existing medical conditions, concomitant drug use or other suspect components of the product in question.

The complementary medicines industry continues to grow, and as well as herbal products, we are interested in any reports of adverse reactions to other alternative products.

Moxifloxacin: Black triangle, black spot?

(*Annals of Pharmacotherapy* 2005; **39**: 361-4)

Prescribing in patients on anticoagulant therapy should be undertaken carefully; in the absence of evidence of safety, a potential for interaction should be assumed.

INR was increased in five patients on warfarin, who had all started moxifloxacin about 5 days (range 3-7) days before presentation. Two patients were admitted to hospital, with one suffering significant gastrointestinal haemorrhage. Similar interaction onsets have been described for other quinolone antibiotics, after similar delays.

This is the second such case series of moxifloxacin interactions with warfarin, the first being published in 2003 (*Eur J Intern Med* 2003; **14**: 255-7).

Many drugs that interact with warfarin compete for cytochrome P450. Moxifloxacin does not, and was thought unlikely to interact with warfarin. A small study in healthy volunteers after a single dose of warfarin supported that erroneous view.

Currently, the BNF only lists ciprofloxacin, nalidixic acid, Norfloxacin, and ofloxacin as quinolones that may enhance the anticoagulant effect of coumarins. They are given a black spot (●) – the symbol indicating interactions that are potentially hazardous and where combined treatment should be avoided or undertaken with caution.

Moxifloxacin should be added to this list.

We welcome reports of any drug interactions with anticoagulants, particularly those related to the use of new (▼) drugs, such as moxifloxacin (Avelox®).

Grapefruit Forethought

(NEJM 2005: **352**; 2211-2221)

A recent review has reviewed drug interactions with grapefruit juice. The phytochemicals in grapefruit juice are though to inhibit the action of cytochrome P450 CYP 3A4 in the intestine, and in repeated doses, in the liver.

Most interactions cause an increasing drug concentration (for example carbamazepine concentrations can be raised by 40% with a single glass of grapefruit juice), but the concentrations of some drugs (fexofenadine) can be reduced.

UK sales of chilled, high quality and natural juice have increased by 60% over the last two years. The public's passion for fruit juices, as part of a healthy lifestyle, is unlikely to decline. In the future novel fruit juices may be promoted to have specific health benefits. Coca-Cola have recently been given initial

approval to market fruit juices containing phytosterols as cholesterol-lowering products.

In recent months the CSM has advised on the potential for interactions between cranberry juice and warfarin. Evidence also exists that apple and orange juice interfere with drugs, by inhibiting polypeptides involved in the transport of drugs in the gut.

The West Midlands Centre for Adverse Drug Reaction Reporting has yet to receive any reports of drug interactions with fruit juices or related products. Considerable detective work may be needed to discover an interaction between a drug and a foodstuff. We welcome any such reports.

Sparkling water?

We have recently received a report of luminous urine associated with lercandipine (Zandip®). A search of the literature reveals no previous cases of luminescence upon micturition, although polyuria is listed as a rare adverse effect in the manufacturer's Summary of Product Characteristics.

We welcome your reports of unusual adverse drug reactions. Such reports can cast further light on the use of medicines.

Xenical® (orlistat) practical problems

We have recently received a report concerning the use of orlistat in a stoma patient. Two weeks use of orlistat led to an oily discharge associated with diarrhoea. Stoma management became difficult and a skin reaction occurred around the stoma area. This reaction was deemed to have caused a significant disability to the patient.

Oily discharge and oily stools are a very common adverse reaction to orlistat, and are listed in the Summary of Product Characteristics. No specific warnings are given about the use of orlistat in stoma patients.

Xenical® is not a black triangle drug and oily discharge is not usually considered a serious reaction. However, this patient suffered marked disability from the reaction.

The West Midlands Centre for Adverse Drug Reaction Reporting welcomes reports, which highlight adverse reactions that are made more serious by patient's particular circumstances.

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** and the entire list of about 220 intensively monitored drugs from our website (http://www.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
brimonidine and timolol	▼ Combigan®	glaucoma
testosterone gel	▼ Testim®	male hypogonadism
onlanzapine injection	▼ Zyprexa®	rapid control of agitation in schizophrenic patients

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