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Resources available to you on the Medsafe web site, under the Health Professionals section:

- Data sheets
- Prescriber Update articles
- Adverse reactions reporting
- Consumer medicine information (CMI)

and more
Notice to all prescribers

If you or your colleagues are not receiving these hard-copy issues of Prescriber Update by mail, then forward your name and postal address to the Editor (contact details on page 28). There is no cost for joining the Prescriber Update mailing list and your details will be used only for this purpose.

What is CARM?

The Centre for Adverse Reactions Monitoring (CARM) based in Dunedin is the central national repository for adverse reaction reports. CARM is contracted by Medsafe to collect voluntary reports of adverse reactions to medicines (including vaccines and blood products), herbal products and dietary supplements. CARM is responsible for collating and analysing these reports, which are submitted by health professionals, consumers and pharmaceutical companies. A medical assessor evaluates each report received by CARM to determine whether there is an association between the adverse reaction and a medicine or dietary supplement, and the strength of any association. CARM responds to each report submitted and gives an indication of the number of similar reports in New Zealand.

The CARM database holds over 50,000 reports from around New Zealand, providing a local pattern of adverse reactions to medicines. These reports also contribute to international knowledge of pharmacovigilance because they are pooled in the World Health Organisation’s (WHO) database for adverse reactions. CARM monitors its database for patterns, clusters and unusual events that could have significance for medicines safety and prescribing practices in New Zealand.

CARM also runs the Intensive Medicines Monitoring Programme (IMMP), which targets specific medicines. The purpose of the IMMP is to identify previously unrecognised adverse reactions to new medicines. It also develops adverse reaction profiles for these medicines, as well as measuring the incidence of, and characterising, reactions of clinical concern.

What is MARC?

The Medicines Adverse Reactions Committee (MARC) is a Ministerial advisory committee (i.e. appointed by, and advisory to, the Minister of Health), which makes recommendations on appropriate action to be taken on medicine safety issues.

Members of the Committee are practising medical practitioners in a range of speciality areas, including general practice. The MARC meets four times a year to review published material, as well as all fatal reports and selected reports of significant, unusual or serious reactions reported to CARM. The Committee also obtains comment from New Zealand specialists, reports from pharmaceutical companies, and regular publications from the WHO and overseas regulatory bodies.

After considering material at its meetings, the MARC may recommend that Medsafe alert prescribers to an adverse reaction through an article in Prescriber Update or a ‘Dear Doctor’ letter. The MARC may also recommend that the pharmaceutical company update the data sheet with advice to improve the safe use of a medicine. Other recommendations made by MARC can include providing comment to Pharmac or a health professional body.

Key to Prescriber Update articles

To assist readers in knowing the origin of articles published by Medsafe, these symbols will appear next to the article title, where relevant:

- **Adverse Drug Reaction Update** articles are written in response to adverse reaction reports lodged with the Centre for Adverse Reactions Monitoring (CARM) and material in the international literature. These articles may also be written to alert prescribers and pharmacists to potential problems with medicines.

- **MARC Prescribing Advice** articles are recommendations from the Medicines Adverse Reactions Committee (MARC) in response to medicine safety issues and overseas experiences.
Can Patients Stomach Cox-2 Inhibitors?

Dr Ruth Savage, Medical Assessor, Centre for Adverse Reactions Monitoring, Dunedin

This article was published on the Medsafe web site and e-mailed to electronic Prescriber Update subscribers in June 2002.

Adverse reaction reports and epidemiological studies suggest that cyclo-oxygenase-2 (COX-2) inhibitors cause gastroduodenal ulceration and subsequent complications. The risk, however, is halved compared with conventional non-steroidal anti-inflammatory agents (NSAIAs). Case reports suggest that COX-2 inhibitors, like NSAIAs, may exacerbate inflammatory bowel disease and cause intestinal strictures. As with NSAIAs, COX-2 inhibitors should be withdrawn in patients with significant gastrointestinal symptoms, pending investigation.

New Zealand reports for COX-2 inhibitors include a high proportion of gastrointestinal adverse effects

Gastrointestinal adverse effects account for about 30% of the COX-2 inhibitor reactions reported to the Centre for Adverse Reactions Monitoring (CARM). There are 65 reports of adverse gastrointestinal effects attributed to celecoxib, 17 of which are serious. These include melaena, gastroduodenal ulcer, intestinal perforation and three deaths. All except two patients had at least one risk factor, other than use of a COX-2 inhibitor, for gastroduodenal ulceration. Fourteen patients were aged 75 years or older. Gastrointestinal reactions have also been reported with rofecoxib.*

Gastrointestinal toxicity reduced by COX-2 inhibitors but not abolished

The COX-2 inhibitors exert their therapeutic effect by inhibiting the production of prostaglandins involved in inflammation. At therapeutic doses they have little or no inhibitory effect on cyclo-oxygenase-1, which is expressed in many tissues and is necessary for the production of prostaglandins that protect the mucosa of the upper gastrointestinal tract. It is therefore expected that COX-2 inhibitors will have reduced gastroduodenal toxicity compared with conventional NSAIAs.

Studies of clinical importance are those that assess the risk of symptomatic ulcers, and bleeding and perforated ulcers. A meta-analysis* of randomised trials of rofecoxib and a prospective study* of rofecoxib and naproxen in 8076 patients (the VIGOR trial) each showed a 50% reduction in risk of peptic ulcer complications and/or upper gastrointestinal bleeding compared with their NSAIA comparators. A large prospective study* of celecoxib compared with diclofenac and ibuprofen (the CLASS trial) showed a similar reduction in risk for ulcer complications although this was not significant. The reduction in risk was significant when patients with symptomatic ulcers were included in the analysis.

These studies* indicate that COX-2 inhibitors do carry an increased risk of gastroduodenal ulcer complications but this is less than with conventional NSAIAs. Since a number of case-control studies* have indicated an approximately 4-fold increase in risk of gastroduodenal ulcer complications with conventional NSAIAs compared with no NSAIA use, it can be assumed from the above studies* that the increase in risk with the COX-2 inhibitors is approximately 2-fold. However, some of this benefit may be lost if low-dose aspirin is taken concurrently. The CLASS study* showed that the risk with celecoxib was greater when low-dose aspirin users were included in the study.

The adverse reaction reports to CARM suggest serious upper gastrointestinal reactions occur predominantly in elderly patients and those with other risk factors. It is likely that this observation in part reflects preferential prescribing of COX-2 inhibitors to at-risk patients. However, a recent report* from the United Kingdom indicates that

* At the time of this data analysis, the use of celecoxib in New Zealand was double that of rofecoxib.
most cases of serious gastroduodenal disease attributed to conventional NSAIAs also occur in patients with other risk factors. It is not known what degree of risk reduction is achieved when switching high-risk patients from NSAIAs to COX-2 inhibitors. The studies described above did include elderly patients and those with a history of ulcer, so some reduction in risk in these patient groups is possible.

**Using lower doses of NSAIAs may also reduce harm**

When deciding whether to use a COX-2 inhibitor, also consider whether more cautious prescribing of a conventional NSAIA would instead be appropriate. In the above studies, the maximum doses of conventional NSAIAs were used as comparators. It has been shown that the risk of gastroduodenal ulcer complications increases with the dose of NSAIA. For patients without significant joint inflammation, low doses and intermittent use may be sufficient. NSAIAs, even at low doses, are contraindicated in patients with active or previous gastroduodenal ulceration.

**Avoid COX-2 inhibitors in patients with active gastroduodenal disease**

COX-2 inhibitors should not be prescribed to patients with active gastroduodenal disease. Where there is a clear need for an anti-inflammatory agent, they may be prescribed cautiously for patients with a history of gastroduodenal ulceration. Evidence that there is a small risk of COX-2 inhibitors causing gastroduodenal ulceration suggests co-prescribing of a gastroprotective agent should be considered in patients who have previously had serious gastrointestinal reactions to conventional NSAIAs.

**Adverse effects on the large intestine have been reported**

There are two reports in the literature of exacerbation of inflammatory bowel disease with celecoxib. Also a 46-year-old woman developed diaphragm-like strictures of the colon while taking celecoxib. Conventional NSAIAs are also known, on rare occasions, to cause ulceration, haemorrhage and diaphragm-like strictures of the distal small intestine and large intestine.

**Use lowest possible dose and discontinue if symptoms of gastrointestinal toxicity occur**

In order to reduce gastrointestinal toxicity, both COX-2 inhibitors and conventional NSAIAs should be prescribed at the minimum effective dose. Unless there is ongoing inflammatory joint disease, they should preferably be used short-term or intermittently. Where strongly indicated, COX-2 inhibitors may be prescribed to patients with a past history of gastroduodenal disease, and gastroprotection should be considered. To avoid progression of adverse effects in the upper and lower gastrointestinal tract, patients should stop taking NSAIAs and COX-2 inhibitors, pending investigation, if pain, bleeding, signs of obstruction or altered bowel habit occur.

Competing interests (author): none declared.

Correspondence to Dr Ruth Savage, CARM, PO Box 913, Dunedin.

**References**

Evidence from Australian adverse reaction reports

Evidence for the combination of angiotensin converting enzyme (ACE) inhibitors, non-steroidal anti-inflammatory agents (NSAIAs) and diuretics precipitating renal failure comes from the Australian Adverse Drug Reactions Advisory Committee (ADRAC). In 1999 ADRAC noted that in 46 of the 78 reports of acute renal failure, patients were taking one or more of a NSAIA, diuretic or ACE inhibitor; seven patients were taking all three. There are now 56 reports in the ADRAC database of renal failure, or worsening renal failure, associated with celecoxib. Twenty-four of these patients were also taking a diuretic and either an ACE inhibitor or angiotensin II receptor antagonist.\(^2\)

Combination inhibits renal compensatory mechanisms

Hypovolaemic states including dehydration, congestive cardiac failure, impaired renal function and anaesthesia may predispose patients to renal insufficiency by lowering the afferent glomerular arteriolar pressure. In order to maintain glomerular perfusion pressure in these circumstances, renal prostaglandin activity dilates the afferent arterioles, and the renin-angiotensin system is activated leading to constriction of the efferent arterioles. Renal failure may be precipitated by NSAIAs and COX-2 inhibitors impairing renal prostaglandin biosynthesis, and by ACE inhibitors and angiotensin receptor blockers reducing angiotensin II activity.

Avoid the trio in at-risk patients

Some patients with predisposing conditions are likely to require ACE-inhibitors and/or diuretics, and should not be co-prescribed NSAIAs or COX-2 inhibitors. In patients taking all three medicines who become predisposed (e.g. due to dehydration from diarrhoea), NSAIAs and COX-2 inhibitors should be withdrawn, and renal function and plasma potassium concentrations monitored closely. The doses of the other medicines should be adjusted accordingly.

The elderly are particularly susceptible to acute renal failure due to the dangerous trio. Most will have some degree of renal impairment (even with a normal serum creatinine concentration), possibly with renal function as low as 50% of normal. Older patients are also prone to diuretic-induced dehydration and hypotension, and their fluid intake is often inadequate.

Competing interests (author): none declared.

References

2. Personal communication, 29 October 2001. Executive Officer, Adverse Drug Reactions Unit, Therapeutic Goods Administration, Australia.
During the first year of monitoring (up to February 2002) of the COX-2 inhibitors in the Intensive Medicines Monitoring Programme (IMMP), 291 reports for celecoxib and 149 for rofecoxib were received. Thirteen of these reports (11 and 2, respectively) are of acute psychiatric events. Some reports gave details of events that were quite dramatic. Confusion, depression and hallucinations were each reported several times, and anxiety and ‘thinking abnormal’ were reported once. Also reported was a patient who suffered an exacerbation of manic depressive psychosis. Most of the patients were elderly and there were more reports involving women, but more women are prescribed these medicines. The acute psychiatric events rapidly resolved upon withdrawal of the COX-2 inhibitor in each case.

A few reports\(^1\,^2\) in the literature suggest that similar reactions occur with the standard non-steroidal anti-inflammatory agents (NSAIAs), but this does not appear to be well known. Practitioners should be alert to the possibility of psychiatric-type reactions with both the COX-2 inhibitors and other NSAIAs. Prescribers are encouraged to continue reporting any such events to the IMMP, in order to facilitate the determination of risk factors.

Competing interests (author): Merck Research Laboratories have provided research grants for the IMMP. Merck Sharp & Dohme (NZ) Ltd are the sponsors of Vioxx™ (rofecoxib).

Correspondence to Dr David Coulter, CARM, PO Box 913, Dunedin. E-mail: david.coulter@stonebow.otago.ac.nz

References

* At the time of this data analysis, the use of celecoxib in New Zealand was double that of rofecoxib.
History of VTE not a contraindication for POPs

The Medicines Adverse Reactions Committee (MARC) advises that the current evidence supports considering progestogen-only oral contraceptives (progestogen-only pills; POPs*) as an option in women with a history of deep vein thrombosis (DVT) or pulmonary embolism (PE), provided the thromboembolic process has resolved. This advice applies even if the thrombotic event occurred with a combined oral contraceptive.

Advice consistent with WHO guidelines

Guidelines released by the World Health Organisation (WHO) in 2000 advocate that for most women with a family or personal history of DVT or PE the benefits of using a POP outweigh the risks, and a POP can generally be used. The guideline also advises that the use of a POP is not recommended in the presence of current venous thromboembolism (VTE) unless other methods are not available or are unacceptable. However, the MARC considers that POPs are an absolute contraindication in women with a current thromboembolic process.

The WHO guidelines make no distinction between minor and major surgery, and recommend that POPs can continue to be used for women undergoing any surgical procedure. Where there is prolonged immobilisation following surgery, the guidelines advise that it is generally appropriate to continue POP use.

Based on this advice, the MARC suggests that when determining the most appropriate oral contraceptive, a POP may also be considered for women with other risk factors that put them at a high risk of VTE with a combined oral contraceptive, especially for those with more than one risk factor (e.g. family history and BMI > 30).

Only one recent case of VTE with a POP in CARM database

Since 1990, the Centre for Adverse Reactions Monitoring (CARM) has received only one report of VTE with a POP. This was a non-fatal PE in a woman taking the POP, ethynodiol. The woman was obese and the PE developed following severe anaphylaxis due to general anaesthesia. Because of the presence of risk factors for VTE, the use of the POP may not have contributed to the event.

This single New Zealand case of VTE with the POPs compares with 32 cases of PE and 48 of other venous thrombotic events with the combined oral contraceptives in the period from February 1996 to December 2001.

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* POPs approved in New Zealand are Cerazette™, Femulen™, Microlut™, Microval™ and Noriday™.
Case-control studies find no increase in risk of VTE with POPs

Three case-control studies\textsuperscript{3,4} have examined the risk of VTE with POPs. None found that use of POPs was associated with a significantly elevated risk of VTE. Each of the studies had small case numbers, but one\textsuperscript{2} conducted by the WHO included 21 cases.

With higher doses of progestogens used for non-contraceptive purposes (daily dose 5-30mg compared with 0.03-0.5mg for contraception), Vasilakis et al\textsuperscript{3} and the authors\textsuperscript{5} of the WHO study found the risk of VTE increased. These studies also involved small case numbers.

While all results indicate a need for further studies, at the doses routinely used for contraception, current evidence suggests that there is little or no increase in risk of VTE with POPs. There may be an elevation in risk with higher dose progestogens. Any new information that becomes available on this topic will be reviewed by the MARC, and prescribers will be advised, if necessary.

Competing interests (authors): none declared.

References

NZ fatality following nitrofurantoin-induced interstitial lung disease

The Centre for Adverse Reactions Monitoring (CARM) has received a report of interstitial pneumonitis following long-term use of nitrofurantoin. A 67-year-old female with a history of severe rheumatoid arthritis developed a chronic cough after 20 months of nitrofurantoin therapy taken for severe recurrent urinary tract infections. She continued to receive nitrofurantoin for a further six months before it was discontinued after interstitial lung disease was diagnosed. She died three months later of severe hypoxia.

In the CARM database, 34% of the nitrofurantoin adverse reaction reports involve the respiratory system. Half of these reflect lung tissue damage including nine reports of pulmonary fibrosis. Twenty-six reports for respiratory reactions were as a consequence of chronic nitrofurantoin therapy.

Acute and chronic forms of pulmonary reactions can occur

First described in 1957, pulmonary toxicity with nitrofurantoin is rare with an estimated incidence of 1 in 5,000 first administrations for acute severe disease. Chronic pulmonary reactions are 10-20 times less frequent than acute reactions. However, pulmonary adverse reactions are among those most frequently reported for nitrofurantoin and cover a spectrum ranging from acute to chronic forms. Acute pulmonary reactions typically have hypersensitivity-type features, and usually affect women aged 40-50 years. They occur 1-2 weeks after initiation of nitrofurantoin, and can recur within minutes to hours of subsequent use. Chronic pulmonary reactions mainly involve older persons, are often insidious in onset and associated with therapy of six months or longer. Interstitial lung disease and pulmonary fibrosis may develop.

The insidious onset can result in an erroneous diagnosis of cardiac failure.

Possible immune or toxicity mechanism

The two forms of pulmonary reaction are considered to be different disease entities and the acute type does not necessarily lead to chronic reactions. The acute pulmonary reaction is likely to be caused by an immune reaction of the hypersensitivity type. In the chronic form, the causative role of nitrofurantoin is less clear, but could be via a toxicity mechanism. The majority of pulmonary reactions are not severe, but persisting damage is common with chronic reactions. Mortality has been estimated to occur in 10% of patients affected by either form. There have also been isolated reports of pulmonary haemorrhage and bronchiolitis obliterans organising pneumonia (BOOP) with nitrofurantoin.

Cautious use and monitoring can reduce morbidity

Nitrofurantoin is contraindicated in patients with impaired renal function as there may be an increase in plasma concentration with subsequent toxicity. Care should be exercised in the elderly,
or those with impaired renal function who may also be at increased risk of toxicity. Long-term use of nitrofurantoin should not exceed six months unless the benefits clearly outweigh the risks. The pulmonary condition of patients undergoing prolonged nitrofurantoin therapy should be monitored. This should include careful vigilance for early features of emerging pulmonary toxicity, which may be evidenced by cough or shortness of breath, indicating the need for further investigation. Nitrofurantoin-induced pulmonary injury can present with a diverse range of clinical manifestations, posing a diagnostic challenge. Where there is a high index of suspicion, investigation should include chest x-ray and spirometry.

Nitrofurantoin must be withdrawn at the first signs of pulmonary damage. Evidence indicates that in general there is rapid improvement of clinical symptoms on withdrawal of nitrofurantoin, although x-ray findings resolve slowly and clearing may remain incomplete in 50% of patients. Patients who have experienced pulmonary toxicity with nitrofurantoin should not be re-exposed to this medicine.

**Pulmonary reactions occur with other medicines too**

A number of other medicines have also been implicated in causing significant pulmonary injury. These include methotrexate and amiodarone. The cases reported to CARM are a reminder about the role of nitrofurantoin in the pathogenesis of pulmonary toxicity, and the need for vigilance in patients taking these medicines.

Competing interests (author): none declared.

**Correspondence to Dr Michael Tatley, CARM, PO Box 913, Dunedin. E-mail: michael.tatley@stonebow.otago.ac.nz**

**References**

The Medicines Adverse Reactions Committee (MARC) first initiated the list of *adverse reactions of current concern* in 1994, as a means of bringing particular medicine adverse reactions to the attention of prescribers. The purpose of the list is also to encourage prescribers to report the reactions to the Centre for Adverse Reactions Monitoring (CARM) so that more information can be gathered, and further action taken if necessary. The reports provide a New Zealand perspective on emerging medicine safety issues.

As with any adverse reactions monitoring scheme, analysis can only be based on reports that are received. Prescribers are therefore encouraged to continue reporting adverse reactions to CARM so that the MARC can make the best possible recommendations based on information reflecting the New Zealand situation.

Since initiation, the number of reactions listed has grown, and is revised from time to time. Amendments are made either in response to reactions reported in New Zealand or international pharmacovigilance issues.

**Update**

**Herbal medicines**

These were first listed as *adverse reactions of current concern* in October 1996 when CARM received increasing numbers of reports of adverse reactions to herbal medicines. Prior to 1996, there had been 17 reports to CARM for herbal products. This has now grown to a total of 153 reports encompassing 172 products. These reports cover a range of products, such as echinacea and bee pollen, hence the term ‘herbal medicines’ has now been widened to ‘complementary and alternative medicines’ (CAMs), to include any medicines containing plant or animal extracts.

In 72 of the reports the CAM was the sole suspected agent, and for 21 reports more than one CAM was suspected of causing the adverse reaction. The most common reports are for bee products (29) and St Johns Wort (17).

Obvious hypersensitivity reactions are reflected in at least 28% of all reports (n=43) for CAMs, and drug interactions account for 15% (n=23). The most common reactions include the skin (51), neuro-psychiatric (40), alimentary (34), hepatic (26) and cardiovascular (25). Of note, there are 14 reactions affecting the haematological system, nine endocrine/metabolic reactions and five uterine bleeding disorders.

These findings highlight the potential for adverse events with complementary and alternative medicines, some of which are both severe and serious. These include one death, four reports of anaphylaxis, two of hepatic failure and seven reports of abnormal bleeding disorders.

The presence of hypersensitivity reactions, and in recent time increasing numbers of reports suggesting interactions with prescribed (or ‘conventional’) medicines, highlight the ongoing need for caution regarding the use of CAMs. Prescribers are encouraged to be mindful of potential use by patients, and to continue reporting any suspected events with complementary and alternative medicines so more can become known.

Please report all cases of adverse reactions in the following table, to the Centre for Adverse Reactions Monitoring (CARM), PO Box 913, Dunedin. The reporting form inside the back cover of *Prescriber Update* can be used, or the form downloaded from either the CARM or Medsafe web sites: www.otago.ac.nz/carm or www.medsafe.govt.nz/Profs/adverse.htm

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**ADVERSE REACTIONS OF CURRENT CONCERN**

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**ADVICE**

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### About the IMMP

The purpose of the Intensive Medicines Monitoring Programme (IMMP) is to identify previously unrecognised adverse reactions to new medicines. It also develops adverse reaction profiles for these medicines, as well as measuring incidence and characterising reactions of clinical concern. In addition, the IMMP is able to identify any high-risk groups amongst the patients being treated. The results of IMMP findings are used to enhance the safe use of medicines.

### What to report

Successful assessment of the significance of events depends on you reporting all events occurring with IMMP medicines, including adverse reactions and random clinical incidents. Please report:

- all new events including common minor ones
- any change in a pre-existing condition
- abnormal changes in laboratory test results
- accidents
- all deaths and causes
- possible interactions.

### Where to report

Please report all cases of adverse events occurring with IMMP medicines to the Centre for Adverse Reactions Monitoring (CARM), PO Box 913, Dunedin. The reporting form inside the back cover of *Prescriber Update* can be used, or the form downloaded from either the CARM or Medsafe web sites: www.otago.ac.nz/carm or www.medsafe.govt.nz/Profs/adverse.htm
The medicines currently being monitored are (no changes since the April 2002 issue of Prescriber Update):

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<tr>
<th>Medicine</th>
<th>Proprietary name/s</th>
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<td>Celecoxib</td>
<td>Celebrex</td>
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<td>Clozapine</td>
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<td>atypical antipsychotic</td>
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<td>Entacapone</td>
<td>Comtan</td>
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<td>Levonorgestrel intrauterine system</td>
<td>Mirena</td>
<td>progestogen-releasing intrauterine system</td>
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<td>Montelukast</td>
<td>Singular</td>
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<td>Serzone</td>
<td>antidepressant / 5HT2 blocker</td>
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<td>Vioxx</td>
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Follow-up only:
New patients are no longer being added to the cohorts for copper IUCD (Multiload Cu 375™), eformoterol (Foradil™, Oxis™) and salmeterol (Serevent™). However, follow-up of existing patients is continuing.
# Reporting form for Adverse Reactions to Medicines, Vaccines and Devices and all Clinical Events for IMMP

## PATIENT DETAILS

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## ALL MEDICINES IN USE – ASTERISK SUSPECT MEDICINE(S)

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<th>Date Stopped</th>
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## DESCRIPTION OF ADVERSE REACTION OR INCIDENT

Date of Onset: 

## OTHER FACTORS

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## REPORTING DOCTOR/PHARMACIST

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Send completed form to CARM

Post: Freepost 112002, CARM, PO Box 913, Dunedin  or  Fax: (03) 479 7150
ADVERSE REACTIONS REPORTING GUIDELINES

Please do not hesitate to report any suspect reaction of clinical concern. The following general guidelines apply.

Report adverse reactions to:

- All medicines
- Vaccines
- “Over-the-counter” (OTC) medicines
- Herbal, complementary and alternative remedies

Report adverse reactions and interactions that are:

- serious
- adverse reactions of current concern¹

Report all adverse reactions to new medicines and all events to IMMP medicines.²

Report serious allergic reactions so that a danger or warning can be entered against the patient’s name in the national health database.

If in doubt, report.

To report: Use the form overleaf or the card supplied with New Ethicals Catalogue.

Or: The form can be downloaded from www.otago.ac.nz/carm or www.medsafe.govt.nz/profs/adverse.htm

Mail the form to: Freepost 112002
The Medical Assessor
Centre for Adverse Reactions Monitoring
PO Box 913, Dunedin

Or fax it to: (03) 479 7150

Phone: (03) 479 7247

Email: carmnz@stonebow.otago.ac.nz

Web site: www.otago.ac.nz/carm

¹ The list of adverse reactions of current concern is on page 27.
² The list of medicines in the Intensive Medicines Monitoring Programme (IMMP) is on page 28.