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Prescriber Update

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FROM THE EDITOR

Keep up with the news

- Prescribers are entitled to receive a free copy of *Prescriber Update* by post – supply your name and address to the Editor (contact details on page 28). Each pharmacy also receives a copy of *Prescriber Update*.
- If your postal address has recently changed, please notify the Editor.
- For all health professionals, Medsafe offers a free e-mail alert service for new Pre*scriber Update* articles and other safety-related medicine information – go to www.medsafe.govt.nz/profs.htm and click on where it says "Click here to subscribe to Prescriber Update Previews" in the centre of the screen. Complete and submit your details to receive e-mails with hyperlinks to new articles (and other relevant information) published on the Medsafe web site.

Internet prescribing – MCNZ statement updated

In June 2006, the Medical Council of New Zealand (MCNZ) issued their updated *Statement on use of the internet and electronic communication*. This *Statement* defines the appropriate use of the internet and e-mail by doctors. It also reiterates that no doctor is permitted to prescribe medicine to an individual unless it is for the treatment of a patient under his or her care. The MCNZ interprets "under his or her care" as requiring a face-to-face consultation. Prescribers are reminded that any medical advice or treatment provided to a patient who is in another location must meet the same standards as care provided in a face-to-face consultation. Doctors also need to be confident that a physical examination would not add critical information before providing treatment or advice to a patient. The full *Statement* can be obtained from the MCNZ web site (www.mcnz.org.nz).

Free resources available

- Consumer Medicine Information (**CMI**) poster
- **Prescribing Medicines in Pregnancy** – categorisation of risk of medicine use in pregnancy – booklet (4th edition, 1999). For recent updates to this booklet, see www.tga.gov.au/docs/html/medpreg.htm
- Medsafe patient information leaflet on **oral contraceptives and blood clots** (March 2002 update).

To order copies of any of these resources, contact Wickliffe: phone 04 496 2277; fax 03 479 0979; email pubs@moh.govt.nz; or post an order to the Ministry of Health, c/- Wickliffe Ltd. PO Box 932, Dunedin.

Key to *Prescriber Update* articles

To assist readers in knowing the origin of articles published by Medsafe, the symbols below will appear next to the article title, where applicable.

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.

WATCHING BRIEFS

Quick updates, alerts and short reminders about medicine safety issues

Psychiatric reactions with cholesterol-lowering agents

The Centre for Adverse Reactions Monitoring (CARM) in Dunedin is receiving an increasing number of reports of psychiatric reactions occurring with the statins, fibrates and, more recently, ezetimibe. These reports account for up to one-fifth of the total adverse reaction reports for some of these agents. The reactions of particular concern are those of aggressive behaviour; but also memory impairment, as well as mood, cognitive, sleep and perception disorders. In Australia, nine cases of depression and three cases of depressed mood have been reported in association with ezetimibe use; onset within four days of commencing ezetimibe was noted in seven of the cases.[1] Prescribers are asked to consider the cholesterol-lowering agents as a possible causal explanation in patients presenting with psychiatric symptoms.

Reference

1. ADRAC. Ezetimibe and depression – A possible signal. *Aust Adv Drug React Bull* 2006;5(5):19.

Statin reminder – myopathy, rhabdomyolysis, and interactions

Prescribers are reminded of the risk of myopathy and rhabdomyolysis with the statins. CARM continues to receive reports of these adverse events. Patients should be monitored for muscle pain, weakness or tenderness especially during the initial months after commencing a statin or increasing the dose. If these symptoms occur the patient should undergo prompt investigation, including the determination of creatine kinase (CK) levels. Statin treatment should be discontinued immediately if myopathy is suspected or diagnosed, or if the CK is more than ten times the upper limit of normal.[1]

Rhabdomyolysis is a severe form of myopathy with muscle breakdown, and may result in renal failure and death. Older age, high statin doses, co-morbidities (e.g. diabetes, hypothyroidism, liver or renal disease), concurrent use of fibrates and/or other interacting medicines can increase the risk of rhabdomyolysis; therefore, these patients require closer monitoring.[1] Simvastatin and atorvastatin are substrates for CYP 3A4, and thus should be discontinued if azole antifungals, macrolide antibiotics, HIV protease inhibitors or nefazodone (i.e. potent CYP 3A4 inhibitors) are indicated. Where co-prescription of amiodarone, fibrates, verapamil or cyclosporin is necessary, only very low doses of simvastatin or atorvastatin should be used.[2] Diltiazem, a weak CYP 3A4 inhibitor, increases the risk of rhabdomyolysis when prescribed with high doses of simvastatin or atorvastatin, or where other risk factors are also present.[3] Suspect co-prescribed medicines in the CARM reports of rhabdomyolysis were cyclosporin, itraconazole and diltiazem.

Patients who are prescribed statins need to be informed of the importance of promptly reporting unexplained muscle symptoms, particularly if accompanied by malaise or fever.[1] Prescribers need to particularly consider those patients at greater risk, as well as the potential for co-prescribed medicines to interact.

References

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2. Merck Sharp & Dohme (New Zealand) Limited. *Lipex (simvastatin) data sheet* 4 May 2005. www.medsafe.govt.nz/Profs/Datasheet/l/Lipextab.htm
3. Gladding P. Potentially lethal interaction between diltiazem and statins [Letter]. *Ann Int Med* 2004;140(8):676.

Watch for muscle disorders with ezetimibe too

Ezetimibe (Ezetrol®; also Vytorin® which contains ezetimibe with simvastatin) is a relatively recent addition to the range of medicines used in the management of hypercholesterolemia. It can be used alone or in combination with a statin.[1] Up to 30 June 2006, CARM had received 44 reports of suspected adverse reactions to ezetimibe. These unexpectedly included one report of suspected myopathy; one of myalgia and muscle weakness; and nine reports of myalgia. Six patients were not taking a statin or fibrate, both of which are known to cause muscle disorders; and recovery was recorded for four of these when ezetimibe was discontinued, including the patient with muscle weakness. Consequently, prescribers are advised to be aware of the potential for ezetimibe to cause myopathy or even rhabdomyolysis, which has been reported overseas.[1] Patients should be advised of this risk and asked to promptly seek medical advice for unexplained muscle pain, tenderness or weakness. As with the other cholesterol-lowering agents, ezetimibe should be immediately discontinued if myopathy is suspected or diagnosed.[1] Prescribers are encouraged to report these adverse reactions so that more data can be gathered and possible risk factors identified. It is currently unclear how or why ezetimibe causes muscle disorders, as its mechanism of therapeutic action differs from that of the statins and fibrates.

Reference

1. Merck Sharp & Dohme (New Zealand) Limited. *Ezetrol (ezetimibe) tablets data sheet* 23 November 2005. www.medsafe.govt.nz/profs/Datasheet/e/Ezetroltab.htm

Terbinafine: serious hepatic and haematological reactions

Prescribers are reminded that the oral antifungal agent terbinafine (Lamisil®, Terbafin®, Apo-Terbinafine®) can cause serious side effects such as agranulocytosis, hepatic failure and Stevens-Johnson syndrome.[1] Case reports to CARM in the last five years include nine reactions that led to hospital admission. Another two cases were life-threatening, consisting of agranulocytosis in one patient, and in the other neutropenia with elevated hepatic enzymes and ulcerative stomatitis. Serious adverse reactions reported include exfoliative dermatitis (3 cases), hepatitis (2), neutropenia (2), pustular rash (2) and agranulocytosis (1). Almost all of the adverse reactions occurred within two months of commencing terbinafine, where duration of treatment was known. In Australia, there have been 16 reports of white blood cell dyscrasias, including seven cases each of agranulocytosis and neutropenia.[2]

Oral terbinafine is not recommended for patients with chronic or active liver disease. Patients should be asked to promptly report symptoms suggestive of impaired liver function or blood dyscrasias, so that clinical investigations can be commenced immediately and terbinafine therapy stopped.[1] To maximise the safety and efficacy of oral terbinafine, prescribers should ensure that the infection is caused by susceptible fungal organisms before prescribing this medicine. An unpublished New Zealand study found that when mycology was performed on patients referred to a dermatologist for treatment of tinea unguium (onychomycosis), 54% of the patients did not have a fungal infection.[3] Non-fungal causes of similar presenting nail symptoms include repeated trauma, psoriasis, lichen planus and vascular disorders.[4] Prescribers are also asked to bear in mind the risks of serious adverse reactions when deciding on the appropriateness of prescribing oral terbinafine for asymptomatic fungal infections.

References

1. Novartis New Zealand Limited. *Lamisil (terbinafine) tablets data sheet* 15 February 2006. www.medsafe.govt.nz/profs/Datasheet/l/Lamisiltab.htm
2. ADRAC. Life-threatening blood dyscrasias with oral terbinafine. *Aust Adv Drug React Bull* 2006;25(4):15.
3. Personal communication, 10 August 2006. Dermatologist, Hamilton.
4. Scher RK, Baran R. Onychomycosis in clinical practice: factors contributing to recurrence. *Br J Dermatol* 2003; 149(Suppl 65):5-9.

Care needed with liquid paracetamol dosing advice for children

Prescribers are asked to be aware that there is a range of strengths of liquid paracetamol products available for purchase by consumers. The strengths are:

- 50mg/ml – intended for infants aged 3-12 months [NB. not funded]
- 120mg/5ml (equivalent to 24mg/ml) – intended for children aged 3 months-5 years
- 250mg/5ml (equivalent to 50mg/ml) – intended for children aged 1 year-12 years and older, as well as adults.

To avoid the risk of inadvertent overdosing, prescribers and pharmacists should always clarify with consumers what strength of liquid paracetamol product they are using – this information is specified on the bottle label. Don't rely on other descriptions such as colour, flavour or product name (e.g. "Junior" or "Infant") to identify the strength of the paracetamol liquid. There are anecdotal reports of prescribers giving dosage advice on the basis of the colour of the product, believing it to be the 120mg/5ml (i.e. 24mg/ml) strength when in fact the consumer has a 50mg/ml strength product. This can result in infants receiving double the recommended dose of paracetamol.

Bisphosphonates and osteonecrosis of the jaws

An article on the dental practice of tooth removal in patients taking oral alendronate was published in the June 2006 issue of *NZDA News*, a publication of the New Zealand Dental Association. A copy of this article can be viewed at www.nzda.org.nz/NZDANEWS_June06.pdf

Increased risk of bleeding with SSRIs

There is evidence from observational studies and case reports that the use of antidepressants, especially selective serotonin reuptake inhibitors (SSRIs), is associated with an increased risk of bleeding due to blockade of serotonin reuptake in platelets and subsequent platelet dysfunction.[1] Various haemorrhagic adverse effects have been reported with the SSRIs, including bruising, purpura, epistaxis, haematoma, vaginal bleeding, peri-operative bleeding and gastrointestinal bleeding.[1-3]

All SSRIs exhibit anti-platelet properties and all have been implicated in bleeding events.[1] A case-control study found that those antidepressants with a higher degree of serotonin reuptake inhibition (such as SSRIs) were significantly associated with an increased risk of hospital admission for abnormal bleeding.[1]

Evidence shows that the risk of bleeding is higher when SSRIs are used concomitantly with other medicines known to increase the risk of bleeding, such as NSAIDs, aspirin, warfarin or low molecular weight heparins.[1-3] SSRIs should therefore be used with caution in patients concomitantly treated with such medicines; in patients with a known tendency for bleeding; and those with predisposing medical conditions. Pharmacological gastroprotection should be considered for high-risk patients.[1]

Following a Medicines Adverse Reactions Committee review in 2005 of the risk of abnormal bleeding with SSRIs, all of the New Zealand data sheets for SSRIs have been updated to include warnings about this potential adverse reaction.

References

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2. Meijer WEE, Heerdink ER, Nolen WA, et al. Association of risk of abnormal bleeding with degree of serotonin reuptake inhibition by antidepressants. *Arch Intern Med* 2004;164:2367-2370.
3. Paton C. Ferrier IN. SSRIs and gastrointestinal bleeding. *BMJ* 2005;331(7516):529-530.

DEXTROPROPOXYPHENE-PARACETAMOL COMBINATION PRODUCTS AND RISK OF OVERDOSE

ADR UPDATE

Medsafe Pharmacovigilance Team

This article was published on the Medsafe web site and e-mailed to electronic *Prescriber Update* subscribers in October 2006.

To enhance the safe use of dextropropoxyphene-paracetamol combination products, changes to the prescribing information have been made. These combination products are now indicated only for the relief of chronic pain of moderate severity in patients who have not adequately responded to, or not tolerated, therapeutic doses of alternative analgesics. The maximum daily dose is eight tablets but lower doses may be adequate for some patients. Concurrent use of alcohol or other paracetamol-containing products is contraindicated, and patients should be counselled accordingly and also reminded not to exceed the recommended dose.

Safety reviewed by MARC

In 2005, Medsafe and the Medicines Adverse Reactions Committee (MARC) undertook a review of the risk of overdose with dextropropoxyphene-paracetamol combination products, such as Capadex® and Paradex®. Fatalities have occurred following intentional and accidental overdose, even with low numbers of tablets, and when normal doses have been taken concurrently with alcohol or other CNS depressants. The combination of paracetamol and dextropropoxyphene carries an overdose risk of rapid-onset respiratory arrest and cardiac arrhythmias due to the dextropropoxyphene component, as well as latent onset of paracetamol-induced hepatic necrosis.[1] In New Zealand, between January 2001 and December 2002, there were 92 deaths from opioid poisonings. Sixteen of these involved dextropropoxyphene, of which six deaths were unintentional.[2]

Part of the MARC's review involved consultation with healthcare professionals and patient support organisations, which provided opinions that there is still perceived to be a clinical need for these products for some patients in the treatment of chronic pain.

Updated prescribing information to improve safety

As a result of the MARC's review, and in order to manage the risks associated with these products, significant changes have been made to the prescribing information for Capadex and Paradex.[3,4] These changes include:

- Narrowing of the indication to the "relief of chronic pain of moderate severity".
- Restriction to second-line therapy for patients who have inadequately responded to, or have not tolerated, therapeutic doses of alternative analgesics.
- Restriction of the recommended dose to 2 tablets up to every 4 hours, with a maximum daily dose of 8 tablets (this represents 2.6g of paracetamol). The dosage should be reduced in patients with hepatic or renal impairment and in the elderly.

For some patients, the time interval between doses can be increased and the total daily dose reduced without compromising pain control.

Avoid concurrent use with alcohol or paracetamol-containing products

Prescribers are reminded that concurrent use of alcohol or other paracetamol-containing products is contraindicated. Dextropropoxyphene-paracetamol combination products should not be prescribed for patients who are suicidal or prone to medicine dependence, and should be prescribed with caution for those patients taking anxiolytics or antidepressants.

Remind patients to adhere to usage instructions

Prescribers and pharmacists should inform patients who have been prescribed a dextropropoxyphene-paracetamol combination product not to exceed the recommended dose; to avoid alcohol; not to take other paracetamol-containing products; not to give their tablets to anyone else; and that unwanted tablets should be destroyed or returned to a pharmacy as soon as possible after completing treatment.

Medsafe and the MARC will continue to monitor the safety of these products.

Competing interests (authors): none declared.

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1. Medicines and Healthcare products Regulatory Agency (MHRA), United Kingdom. *Co-proxamol overdose* 19 May 2005. www.mhra.gov.uk (accessed 26 Sept 2006).
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4. PSM Healthcare Ltd. *Paradex (dextropropoxyphene napsylate 50mg and paracetamol 325mg) tablets data sheet*. 6 April 2006. www.medsafe.govt.nz/profs/Datasheet/p/Paradextab.htm

EVIDENCE FOR TRAMADOL-WARFARIN INTERACTION

ADR UPDATE

Ruth Savage, Medical Assessor, CARM, New Zealand Pharmacovigilance Centre, Dunedin

This article was published on the Medsafe web site and e-mailed to electronic *Prescriber Update* subscribers in October 2006.

Local and international case reports provide evidence of an interaction between oral tramadol and warfarin in some individuals, leading to an elevated International Normalised Ratio (INR) and in some instances bruising or haemorrhage. The mechanism has not been determined. The interaction usually occurs 3-4 days after tramadol is commenced in patients stabilised on warfarin. The decrease in INR after tramadol is withdrawn may take several days. Where it is necessary to prescribe tramadol with warfarin there should be close monitoring of the INR, especially during the first week of treatment with tramadol.

CARM reports show marked increases in INR

Up to 31 July 2006, the Centre for Adverse Reactions Monitoring (CARM) had received a total of 116 reports of suspected adverse reactions to tramadol. Three of these reports were of increased International Normalised Ratio (INR), ranging from 7.0 to 12.3 occurring when oral tramadol was given to patients taking warfarin. Two patients were symptomatic: one with petechiae and one with melaena. Onset time after tramadol was commenced was one, two and seven days. A fourth patient taking warfarin was found to have bruising and a haematoma eight days after commencing tramadol.

The extent to which tramadol contributed to the elevated INR in the four patients is not entirely clear as one patient may have taken an incorrect dose of warfarin and the other three were also prescribed antibiotics. However, tramadol seemed the most likely cause in two of these cases.

Published case reports provide further evidence

Firmer evidence of an interaction with oral tramadol can be found in two published case reports.[1,2] A 76-year-old man had been on a stable dose of warfarin for six months when he developed purpura and was found to have an INR of 7.3. He had been taking tramadol 50mg three times daily for one month. There had been no other changes to his prescribed medication, and he had not taken any over-the-counter medicines.[1] A 61-year-old woman on a stable regime of medicines including warfarin had recently finished taking tramadol 50mg six hourly for two weeks. She presented with extensive bruising of the right upper arm, and was found to have an INR of 10.6. Warfarin was withheld for three days until her INR reduced sufficiently for the warfarin to be reinstated, although initially a lower dose was required.[2]

Similar reports in Australia

Case reports published in 2004 by the Australian Adverse Drug Reactions Advisory Committee (ADRAC) detail 11 reports of elevated INR or haemorrhage when tramadol was taken with warfarin.[3] The median onset time after addition of tramadol to stabilised warfarin therapy was four (range 3-7) days, with the exception of one outlier at six weeks. Five reports described recovery within 1-4 days of tramadol being discontinued, with or without reduction in the dose of warfarin. Two patients, aged 76 and 88 years, died of haemorrhagic stroke.

The interaction may occur in a sub-group of patients

In a pharmacodynamic study[4] of the effect of oral tramadol on INR in 19 patients stabilised on phenprocoumon (a coumarin anticoagulant), two patients had clinically significant increases in INR to 6.0 and 7.3, respectively, while taking tramadol. However, the mean difference in INR for all participants did not reach statistical significance.

The mechanism of the interaction is unclear, but these results suggest that the interaction may be associated with a variation in metabolism and that only a sub-group of patients will be affected. This possibility is supported by the small number of case reports in the Australian database compared with total prescriptions for oral tramadol.[3]

Increased INR monitoring necessary when tramadol prescribed with warfarin

Although the mechanism has not been elucidated, there is evidence for an interaction between oral tramadol and warfarin in some, but probably not all, individuals. The CARM case reports, where antibiotics were also implicated, are a reminder that more than one interaction may be occurring. The interaction between tramadol and warfarin is documented in the product information for tramadol.[5-7] It is unclear whether the interaction occurs with injectable tramadol.[3]

Close monitoring of the INR should be undertaken when it is necessary to prescribe tramadol for patients taking warfarin, especially during the first week of treatment with tramadol.

Competing interests (author): none declared.

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2. Sabbe JR, Sims PJ, Sims MH. Tramadol-warfarin interaction. *Pharmacotherapy* 1998;18(4):871-873.
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5. CSL (New Zealand) Limited. *Tramal (tramadol) data sheet* October 2005. www.medsafe.govt.nz/profs/Datasheet/t/TramalcapSRtabinjoraldrops.htm
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ANTI-TNF AGENTS: HEP B'WARE

ADR UPDATE

Medsafe Pharmacovigilance Team

The following information was sent as a letter to rheumatologists, dermatologists and gastroenterologists in November 2006. It was also published on the Medsafe web site and e-mailed to electronic *Prescriber Update* subscribers.

- **Hepatitis B virus (HBV) reactivation has been reported in patients receiving the anti-TNF agents, Enbrel® (etanercept), Humira® (adalimumab), and Remicade® (infliximab).**
- **Patients at risk for HBV infection should be evaluated for evidence of prior HBV infection before anti-TNF therapy is initiated.**
- **Patients identified as carriers of HBV infection should be closely monitored for signs and symptoms of reactivated HBV infection throughout the course of anti-TNF therapy, and for several months following termination of therapy.**
- **Anti-TNF therapy should be discontinued in patients who develop reactivation of HBV infection.**

Agents that inhibit the pro-inflammatory cytokine, tumour necrosis factor (TNF), are used in the treatment of a range of diseases with an immune component. In New Zealand, the anti-TNF agents Enbrel®, Humira®, and Remicade® are licensed for the treatment of rheumatoid arthritis, psoriatic arthritis, and ankylosing spondylitis. In addition, Enbrel is indicated for juvenile chronic arthritis and plaque psoriasis; and Remicade is indicated for Crohn's disease, psoriasis, and ulcerative colitis.

Very rare cases of hepatitis B virus (HBV) reactivation associated with anti-TNF therapy have been reported internationally. In some instances, the reactivation of HBV infection was fatal. In the majority of cases, patients were receiving concomitant treatment with other immunosuppressants; therefore a causal relationship with anti-TNF agents is confounded by the presence of these other medications.

Patients at risk for HBV infection should be evaluated for evidence of prior HBV infection before anti-TNF therapy is initiated. Patients who are carriers of HBV and require treatment with anti-TNF agents should be closely monitored for signs and symptoms of reactivated HBV infection throughout therapy and for several months following termination of therapy. In patients who develop HBV reactivation, the anti-TNF agent should be stopped and effective anti-viral therapy with appropriate supportive treatment should be initiated.

The New Zealand data sheets for Enbrel, Humira, and Remicade have been updated to include the above safety information and are available on the Medsafe web site (www.medsafe.govt.nz/DatasheetPage.htm).

Please report any case of HBV reactivation or other serious or unexpected adverse reactions in patients receiving anti-TNF agents to: CARM, NZ Pharmacovigilance Centre, PO Box 913, Dunedin. Such post-marketing reports are valuable in enabling a more accurate quantification of risk and in providing a New Zealand perspective on emerging medicines safety issues.

ADVERSE REACTIONS OF CURRENT CONCERN

MARC Rx ADVICE

The Medicines Adverse Reactions Committee (MARC) initiated the list of *adverse reactions of current concern* to bring particular medicine adverse reactions to the attention of prescribers. The intention is to encourage prescribers to report these 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.

Please report **all cases** of the following adverse reactions to: CARM, NZ Pharmacovigilance Centre, PO Box 913, Dunedin. Use the reporting form inside the back cover of *Prescriber Update*, or download the form from the CARM or Medsafe web sites: www.otago.ac.nz/carm or www.medsafe.govt.nz/Profs/adverse.htm

Medicine/s	Adverse reactions of current concern	*Prescriber Update* reference
Complementary and alternative medicines*	all adverse reactions	Vol.23(2), July 2002 & No.13, Oct 1996
Leflunomide	all adverse reactions	Vol.27(1), June 2006 & Vol.26(2), December 2005 & Vol.25(1), May 2004
Pioglitazone and Rosiglitazone	all adverse reactions	Vol.27(1), June 2006

* includes herbal medicines, bee products, homoeopathic products, dietary supplements, minerals, and any other medicines containing animal or plant extracts.

INTENSIVE MEDICINES MONITORING PROGRAMME

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.

Which medicines are monitored?

Medicines of a new class may be added to the IMMP so that unknown adverse effects can be identified as soon as possible. Medicines may also be included in the programme if they are similar to other medicines for which safety concerns exist. The medicines currently being monitored are listed in the table below.

Medicines currently monitored by the IMMP

Medicine	Brand name/s
Clozapine	Clozaril, Clopine
Levonorgestrel intrauterine system*	Mirena
Olanzapine	Zyprexa
Quetiapine	Seroquel
Risperidone	Risperdal
Sibutramine*	Reductil

* New patients are no longer being added to the cohorts for these medicines because sufficient numbers of patients have already been recruited. However, follow-up of existing patients is continuing, which means that adverse event data are still being collected for these medicines. Therefore, prescribers may receive follow-up questionnaires asking about adverse events experienced by their patients taking an IMMP medicine. IMMP encourages prescribers to complete the questionnaires because their participation is a valuable contribution to patient safety.

What to report

Please report **all clinical events** in patients taking IMMP medicines, including:

- any suspected adverse reaction
- deaths (including cause if known)
- any new clinical events, even if minor or common
- accidents
- change in a pre-existing condition
- abnormal changes in laboratory test results
- possible interactions.

Where to report

Please report all adverse events occurring with IMMP medicines to: IMMP, NZ Pharmacovigilance Centre, PO Box 913, Dunedin. Use the reporting form inside the back cover of *Prescriber Update*, or download the form from either the NZ Pharmacovigilance Centre or Medsafe web sites: www.otago.ac.nz/carm or www.medsafe.govt.nz/Profs/adverse.htm

What to tell patients prescribed IMMP medicines

Please remember to tell patients that they have been prescribed a monitored medicine. This means the IMMP receives details of their prescriptions and that their doctor may be asked for clinical information on the patient's experience whilst taking this medicine. If possible, an explanatory IMMP leaflet should be given to the patient (available from the IMMP, NZ Pharmacovigilance Centre, PO Box 913, Dunedin).

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* Comprise the Medsafe Pharmacovigilance Team

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Medsafe web site: www.medsafe.govt.nz

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CARM
CENTRE FOR ADVERSE REACTIONS MONITORING

Fax: (03) 479 7150
Phone: (03) 479 7247

Reporting form for Adverse Reactions to Medicines, Vaccines and Devices and all Clinical Events for IMMP

PATIENT DETAILS

HP3442

Surname:	First Name/s:	NHI No:	
Address:		Date of Birth:	Sex:
		Ethnicity:	

ALL MEDICINES IN USE *ASTERISK SUSPECT MEDICINE/S* Include over-the-counter (OTC) and alternative medicines

Medicine or Vaccine+batch no. (and brand name if known)	Daily Dose	Route	Date Started	Date Stopped	Reason for Use

DESCRIPTION OF ADVERSE REACTION OR EVENT

Date of onset: _____

Recovered ☐ Not yet recovered but improved ☐ Not yet recovered ☐ Unknown ☐ Fatal ☐ - Date of Death: _____

Severe? - Yes ☐ No ☐ Rechallenged? - No ☐ Yes ☐ Result: _____

OTHER FACTORS - Please tick or specify as appropriate

Renal disease ☐ Allergy ☐: _____ Other Medical Conditions: _____

Hepatic disease ☐ Nutritional Suppl or OTC use ☐ : _____ Industrial Chemicals ☐ : _____

REPORTER - Please tick as appropriate: Doctor ☐ Pharmacist ☐ Dentist ☐ Nurse ☐ Other ☐ : _____

Name:

Address:

Signature: _____

Phone: _____ Date: _____

Send completed form to CARM

Freepost 112002, CARM, PO Box 913, Dunedin **or** Fax: (03) 479 7150

ADVERSE REACTIONS

What to report

Please report any suspect reaction of clinical concern. This includes adverse reactions involving:

- Prescription medicines
- Over-the-counter medicines (medicines purchased without a prescription)
- Complementary medicines (herbal medicines, naturopathic and/or homoeopathic medicines, and nutritional supplements such as vitamins and minerals)
- Vaccines.

In particular, please report the following:

- All suspected reactions to NEW medicines
- All Adverse Reactions of Current Concern[1]
- All events to IMMP medicines[2]
- All suspected drug INTERACTIONS
- UNEXPECTED or SERIOUS reactions (including those suspected of causing death, admission to hospital, prolongation of hospitalisation, or birth defects)
- Serious ALLERGIC reactions (to enable a danger or warning to be entered in the national health database so re-exposure can be avoided for that individual).

How to report

Fill in the reporting form, which is available:

- overleaf (inside the back cover of *Prescriber Update*)
- from the CARM web site: http://carm.otago.ac.nz/reporting.asp

On-line reporting is also available on the CARM web site.

Where to report

Send all adverse reaction reports to CARM (Centre for Adverse Reactions Monitoring) in Dunedin.

Post to: Freepost 112002
The Medical Assessor
CARM
University of Otago Medical School
PO Box 913
Dunedin

Fax: (03) 479 7150

Phone: (03) 479 7247

E-mail: carmnz@stonebow.otago.ac.nz

1. The list of *Adverse Reactions of Current Concern* is on page 26
2. The list of medicines in the Intensive Medicines Monitoring Programme (IMMP) is on page 27