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Launch of an electronic adverse reaction reporting tool

An electronic adverse reaction reporting tool has been launched in New Zealand. This tool is designed to facilitate the reporting of adverse drug reactions to the Centre for Adverse Reactions Monitoring (CARM) and uses an online reporting form pre-populated with patient details from the GP practice software.

The World Health Organization rates New Zealand as having the highest number of reports submitted per capita compared to other countries in their programme. Reports from New Zealand are also rated as being of the highest quality. Despite this, international research indicates that at best, only 1 in 10 adverse reactions are being reported in New Zealand.

In addition, research conducted in New Zealand examined the data stored in the Patient Management Systems of 30 General Practices. Of the 725 entries in the medical warnings files that recorded an adverse reaction or allergy to at least one medicine, only 21 were reported to CARM.

Known barriers to reporting include the absence of a prompt to initiate reporting, considering that the reaction is already well known, and finally the time required to manually fill in adverse reaction forms. The adverse reaction reporting tool has been developed to help overcome these barriers.

When the tool is opened it automatically pre-populates the patient's medical history, medicine history, and gives the reporter the option of including laboratory test results. If a vaccine is a suspected medicine, the tool pre-populates the batch number, the date of administration, and how the vaccine was given. Once a description of the reaction is entered, one click on the mouse sends an electronic report to CARM.

Reporters can be assured that the confidentiality of patient and reporter details is maintained in this reporting tool. Although the electronic form is routed through a third party server, the information in the report is only viewed by CARM.

We are hoping that electronic reporting will result in an increase in adverse reaction reports. In addition, providing laboratory and other investigation reports improves the ability of the clinicians reviewing the data to determine whether the medicine is causing the reaction. This will speed up the process of data analysis and improve the identification of safety signals. The tool is also expected to allow for easier reporting of reactions to over the counter medicines and complementary medicines, both of which are under-reported in New Zealand.

This new reporting system is one of the first in the world to deliver direct electronic reporting of adverse reactions to GPs. Use of this system will strengthen the close relationship that exists between prescribers and the medicines safety community.

Isotretinoin – indications and teratogenicity

Isotretinoin is an oral retinoid indicated for the treatment of severe forms of nodulo-cystic acne, in particular cystic acne and acne conglobata. Isotretinoin is indicated in acne that is resistant to therapy. In order to judge its effectiveness in individual patients and reduce the chance of adverse reactions it should not be used with other acne treatments.

Changes to the funding of isotretinoin have widened access for patients to this highly effective therapy; therefore we are taking this opportunity to inform prescribers, who may be unfamiliar with the safety profile of isotretinoin, of its teratogenic effects.

Medsafe is aware that isotretinoin exposure has been responsible for a number of pregnancy terminations in recent years. If exposure to isotretinoin occurs during pregnancy there is a high risk of a deformed infant or foetal death, even if the exposure is only for a short period. Malformation rates of up to 30% are expected in women exposed to isotretinoin in the first trimester of pregnancy. This is compared to a baseline risk of malformation of 3 to 5% in the general population.[1]

As a result of its teratogenicity isotretinoin is contraindicated in women of childbearing potential unless an extensive list of conditions for prescribing are met. For further information on the conditions associated with prescribing isotretinoin, please see the product data sheets at: www.medsafe.govt.nz/profs/Datasheet/dsform.asp.

Internationally various strategies are used to reduce the risk of pregnancy exposure to isotretinoin. Strategies range from prescribing restrictions to extensive risk management systems such as the iPledge system used in the USA. However, the effectiveness of these strategies remains unproven as cases of isotretinoin exposure in pregnancy are still reported.

Medsafe is currently in the process of assessing the risk mitigation strategies used by the manufacturers of isotretinoin products in New Zealand and will advise prescribers of any action as necessary. In the meantime prescribers are reminded to:

- Assess risks and benefits before initiating or continuing isotretinoin treatment.
- Be aware of the conditions that patients need to meet before being treated with isotretinoin. These conditions include the use of at least one & preferably 2 complimentary forms of contraception (including a barrier method).
- Be aware of the risks associated with isotretinoin exposure during pregnancy.
- Report all adverse reactions to CARM.

Medsafe is aware that a decision support tool specifically designed for isotretinoin prescribing is now available through the Best Practice Advisory Centre New Zealand (BPAC^{NZ}). Please contact BPAC for further information.

Reference

1. Berard A, Azoulay L, Koren G, Blais L, Perreault S, Oraichi D. Isotretinoin, pregnancies, abortions and birth defects: a population-based perspective. Br J Clin Pharmacol. 2007; 63: 196-205.

Phosphate containing laxatives – hyperphosphataemia and kidney damage

Medsafe would like to draw prescribers attention to evidence of an increased risk of acute renal failure due to the use of oral phosphate containing laxatives prior to colonoscopy.

Adverse reaction reports include end stage renal failure (requiring dialysis) and renal failure resulting in death.

The Medicines Adverse Reactions Committee (MARC) reviewed this issue at its December 2008 meeting and considers that significant risks exist, particularly renal damage and electrolyte imbalances such as hyperphosphataemia, hypokalaemia and hypocalcaemia. The MARC noted that renal damage typically takes the form of phosphate nephropathy.

The Fleet Phospho-soda Bufffered Saline Mixture is the only phosphate containing oral laxative approved in New Zealand and its data sheet includes the following contraindications:

- Clinically significant impairment of renal function and potentially pre-existing fluid/ electrolyte disturbances.
- Patients at risk of dehydration due to altered senses and/or poor fluid intake.

Risk factors for the development of renal damage following colonoscopy include prior dehydration and comorbid conditions such as hypertension, congestive cardiac failure, diabetes mellitus, liver and renal impairment. Medicines that may predispose patients to phosphate nephropathy include non-steroidal anti-inflammatory drugs (NSAIDs), angiotensin converting enzyme inhibitors (ACEI), angiotensin receptor blockers (ARB), and diuretics.

In order to reduce the risk of dehydration and hyperphosphataemia patients should be encouraged to drink large quantities of fluid during bowel preparation (approximately 750 mL of clear liquid per 45 mL dose followed by 750 mL over the next 10-12 hours).

Products containing alternative active ingredients should be considered for bowel preparation in patients at risk, the elderly and others unlikely to be able to maintain hydration.

Prescribers should consider steps to maintain hydration in at risk patients and may need to monitor renal function and electrolytes.

This risk is discussed in more detail by Markowitz et al (2005)[1]

Reference

1. Markowitz et al. 2005.Acute Phosphate Nephropathy following Oral Sodium Phosphate Bowel Purgative: An Underrecognized Cause of Chronic Renal Failure.2005.*Journal of the American Society of Nephrology*, 16: 3389 – 3396.

Psychiatric reactions with varenicline: interim results from intensive monitoring in New Zealand

Dr Mira Harrison-Woolrych, Director, Intensive Medicines Monitoring Programme

Varenicline (Champix) is the newest smoking cessation medicine available in New Zealand and has been monitored by the Intensive Medicines Monitoring Programme (IMMP) since its introduction here in 2007. The IMMP has recently analysed results for 3389 patients who were dispensed a prescription for varenicline in the first year (1 April 2007 to 31 March 2008) of marketing in New Zealand.

In this interim analysis the IMMP identified a total of 293 reports (for 284 patients) with a total of 538 adverse events occurring while the patient was taking varenicline. These events have been identified from follow-up questionnaires sent to doctors in June 2008 and spontaneous reports submitted to the New Zealand Pharmacovigilance Centre (NZPhvC). The most frequently reported adverse events were psychiatric effects, with a total of 169 events (31% of all events). The most common psychiatric adverse events reported were depression (22 events), insomnia (22), sleep disturbance (13), fatigue (12), vivid/strange dreams (10), nightmares (10), and anxiety (9). There have also been four reports of depersonalisation, four reports of mood swings, four of panic attacks, and two of hypomania/mood elevation.

Depression and Suicidal Ideation

Of the 22 reports of new-onset depression while taking varenicline, 15 were assessed as having a 'probable' relationship (i.e. there was evidence of positive dechallenge) with varenicline and 7 were assessed as having a 'possible' relationship.[1] Three of the patients who experienced depression while taking varenicline also reported suicidal ideation and in two cases this resolved on cessation of the medicine. A further 10 patients experienced a worsening or recurrence of existing depression while taking varenicline. Of these, four recovered on withdrawal of varenicline, with the other six assessed as having a 'possible' relationship with the medicine.

Regarding psychiatric adverse effects, the New Zealand data sheet for Champix includes the following advice: "*Patients and their families should be advised that the patients should stop taking CHAMPIX and contact a health care professional immediately if changes in behaviour, agitation or depressed mood, that are not typical for the patients are observed, or if the patient develops suicidal ideation or suicidal behaviour*".[2]

Withdrawal Symptoms

The IMMP has identified six reports of symptoms following cessation of varenicline which appear to be withdrawal effects. Two patients experienced a withdrawal depression and one of these patients also experienced anxiety. In other patients withdrawal symptoms included agitation, mood swings, cravings, night sweats, insomnia, and taste disturbance. The New Zealand data sheet for Champix includes mention of withdrawal effects and prescribers should advise patients of this possibility.[2]

Prescribers are reminded that patients may also experience psychiatric symptoms such as depression and irritability for many reasons including nicotine withdrawal. Information provided by prescribers in the IMMP follow up questionnaires will help us to evaluate the significance of these possible confounding factors.

Summary of Key Messages for Prescribers:

- Varenicline/Champix continues to be monitored by the IMMP – please inform patients of this when prescribing this medicine.
- Psychiatric reactions have emerged as a potential safety issue with varenicline and patients should be advised accordingly.
- Patients may experience adverse effects after stopping varenicline and should be informed of such possible withdrawal effects.
- Please continue to return all IMMP follow-up questionnaires and other reports of adverse events promptly.

References

1. Kunac DL, Harrison-Woolrych ML, Tatley MV.(2008). Pharmacovigilance in New Zealand: The role of the New Zealand Pharmacovigilance Centre in facilitating safer medicines use *NZ Medical Journal* 121; 1281: 76-89

2. Pzifer Inc.(2009).Data sheet for Champix accessed 30 March 2009 at: www.medsafe.govt.nz/profs/datasheets

Avastin – "off-label" intraoccular administration

An increase in eye-related adverse reactions has been identified following administration of Avastin into the vitreous humour.

Avastin is an antineoplastic agent containing bevacizumab. Bevacizumab is a recombinant humanised monoclonal antibody that selectively binds to and neutrialises the biological activity of human vascular endothelial growth factor (VEGF).

Avastin is approved in New Zealand for the treatment of:

- Metastatic colorectal cancer in combination with fluoropyrimidine based chemotherapy.
- Advanced and/or metastatic renal cell cancer in combination with interferon alfa-2a.

In addition to the indications listed above, Medsafe understands that intraoccular Avastin is also widely used throughout New Zealand for the treatment of neovascular age-related macular degeneration (AMD).

The manufacturer of Avastin has reported two clusters of eye-related adverse reactions following intraoccular administration in Canada (25 reports in total). In addition, five reports of eye-related adverse reactions following the use of intraoccular Avastin have been received in New Zealand. Reports include reactions such as eye inflammation, endophthalmitis, blurred vision, and the presence of "floaters". Although a causal relationship is yet to be proven, the manipulation of Avastin single use vials into multiple aliquots for intraoccular administration may increase the risk of contamination.

Prescribers are reminded that the use of intraoccular Avastin for the treatment of AMD is not approved in New Zealand and constitutes "off-label" use. As adverse reactions to medicines used off-label are under-reported, emerging safety signals can be difficult to identify. Prescribers are asked to report all adverse reactions to CARM.

Medsafe will continue to monitor eye-related adverse reactions associated with the use of Avastin and communicate further advice to prescribers as necessary.

Adverse reactions to topical anaesthetics

Medsafe has recently been made aware of serious adverse reactions resulting from improper use of topical anaesthetics such as lidocaine, amethocaine and prilocaine.

In January 2009, the Food and Drug Administration (FDA) issued a public health advisory about the improper use of topical anaesthetics. This advisory followed reports of adverse events and the deaths of two women who used topical anaesthetics prior to laser hair removal procedures. Both cases involved the use of high concentrations of topical anaesthetic over large areas of the body.

In addition, other international regulatory agencies have also received reports of serious adverse reactions such as methaemoglobinaemia, irregular heartbeat, seizures, coma and breathing difficulties. These reactions have been reported in adults and children when administered for both approved and unapproved indications.

Prescribers are reminded of the following:

- If a topical anaesthetic is required the lowest possible dose should be used.
- Topical anaesthetics should not be applied to irritated or broken skin.
- Children should be monitored during and after the use of topical anaesthetics as they may be at greater risk of experiencing adverse reactions than adults.

Patients who use topical anaesthetics on large areas of their body, or use occlusive wraps or dressings to enhance the effects of topical anaesthetics are more likely to experience serious adverse reactions.

Cough and cold products – an update

MUST NOT BE USED IN CHILDREN UNDER TWO YEARS OF AGE

Healthcare professionals will recall that following a review of the safety and efficacy of cough and cold products in chidren in December 2007, the MARC considered that the risk-benefit profile of these products is unfavourable for children under two years of age.

The MARC recommended that cough and cold products be contraindicated in children under two years of age based on limited evidence for efficacy in this age group, an absence of evidence-based dosing, and evidence of significant toxicity in overdose.

Medsafe has been working together with New Zealand sponsors to amend the product packaging for cough and cold products. Affected products will now include the statement *"Must not be used in children under two years of age"*, or words to this effect.

The packaging amendments are required for all cough and cold products containing bromhexine, brompheniramine, chlorphenamine, dextromethorphan, diphenhydramine, doxylamine, guaifenesin, ipecacuanha, oxymetazoline, phenylephrine, pholcodine, promethazine, pseudoephedrine, triprolidine and xylometazoline. A list of currently marketed cough and cold products (as at 1 March 2009) that require the new warning is provided on the Medsafe web site (www.medsafe.govt.nz/hot/alerts/CoughAndCold.asp).

It is expected that all affected retail stock will include this warning by 1 May 2009 and will either be on the product label or as a sticker affixed to the product. The sticker is a temporary labelling compromise agreed between Medsafe and the New Zealand Self-Medication Industry Association.

Medsafe and the MARC are continuing to review the safety and efficacy of cough and cold products in children over two years of age, and are considering the risks and benefits of these products.

Antiepileptic medicines – increased risk of suicidality

The FDA performed an analysis of reports of suicidality (suicidal behaviour or ideation) from clinical trials of eleven medicines used to treat epilepsy, psychiatric disorders and other conditions (including neuropathic pain). The analysis included 199 placebo-controlled trials involving a total of 43,800 patients.[1]

The FDA stated that patients receiving antiepileptic medicines had approximately twice the risk of suicidal behavior or ideation (0.43%) compared to patients receiving placebo (0.24%). The increased risk of suicidal behavior and suicidal ideation was observed as early as one week after starting the antiepileptic medicine and continued through 24 weeks.

Patients who were treated for epilepsy, psychiatric disorders and other conditions were all at increased risk for suicidality when compared to placebo. There did not appear to be a specific demographic subgroup of patients to which the increased risk could be attributed. The relative risk for suicidality was higher in patients with epilepsy compared to patients who were given one of the medicines for psychiatric or other conditions.

The increased risk of suicidal thoughts or behaviour was generally consistent among the eleven medicines with varying mechanisms of action and across a range of indications. This suggests that the risk applies to all antiepileptic medicines used for any indication.

A separate European review of clinical trial data, published literature and post-marketing spontaneous reports of adverse drug reactions also concluded that any antiepileptic medicines may rarely be associated with a small increased risk of suicidal thoughts and behaviour.[2]

All patients who are currently taking or starting an antiepileptic medicine should be closely monitored for notable changes in behaviour that could indicate the emergence or worsening of suicidal thoughts/behaviour or depression. Healthcare professionals should inform patients, their families and caregivers of the potential for an increase in the risk of suicidality and

should advise patients to seek medical advice immediately if they develop any symptoms suggestive of suicidality.

The data sheets for all antiepileptic medicines approved in New Zealand are in the process of being updated to include this advice.

References

1. Levenson M. 23 May 2008. Statistical review and evaluation: Anti-epileptic drugs and suicidality. Available from: http://www.fda.gov/ohrms/dockets/ac/08/briefing/2008-4372b1-01-FDA.pdf
2. MHRA. August 2008. Antiepileptics: Risk of suicidal thoughts and behaviour. *Drug Safety Update*. 2(1): 2.

Combination use of Angiotensin Converting Enzyme inhibitors (ACEI) and Angiotensin Receptor Blockers (ARB)

The Ongoing Telmisartan Alone and in combination with Ramipril Global Endpoint Trial (ONTARGET) investigated the use of telmisartan (ARB) with ramipril (ACEI)[1] (Lancet 2008; 372: 547-53). The use of telmisartan and ramipril did not result in a reduction in cardiovascular events above that seen with each medicine individually, but did result in a higher incidence of adverse renal events, a faster deterioration in renal function parameters, hypotension, diarrhea, and hypokalaemia.

The applicability of these results to other combinations of ACEIs and ARBs or when used in different indications is not certain. Prescribers are advised only to use an ACEI in combination with an ARB if judged strictly necessary in individual patients and to monitor these patients closely for adverse effects.

Reference

1. Mann JFE, Schmieder RE, McQueen M, et al. Renal outcomes of telmisartan, ramipril, or both, in people at high vascular risk (the ONTARGET study): a multicentre, randomized, double-blind, controlled trial. Lancet 2008; 372:547-53.

Metabolic effects of antipsychotics

Although schizophrenia itself is associated with several adverse metabolic effects it is now clear that all antipsychotics, and in particular some atypical antipsychotics, are associated with adverse effects on weight, blood glucose, and lipid concentrations. All of these adverse effects have long-term consequences in terms of life expectancy.

While the effects of antipsychotics on weight gain may be responsible for the increased risk of diabetes and hyperlipidaemia, a direct effect on glucose metabolism may also occur.

Not all atypical antipsychotics are associated with the same level of risk. Clozapine and olanzapine are considered to cause adverse metabolic effects more frequently than other agents.

Prescribers are advised to monitor all patients taking antipsychotics for adverse metabolic effects.

BPAC[1] have published guidance on appropriate monitoring for patients which includes:

Weight gain
- Measure baseline weight and monthly weights for all patients prescribed atypical antipsychotics or phenothiazines including depot preparations.
- Offer dietary management for obese people (BMI > 30) or those gaining significant weight (≥ 7%) during treatment.

Lipids
- Measure baseline fasting triglycerides and total cholesterol with any antipsychotic, repeated three monthly with atypical agents for the first year of treatment.
- A full lipid profile performed annually as part of routine health.

Glucose
- Consider screening all patients with schizophrenia for diabetes particularly those with risk factors for developing diabetes and those on higher risk drugs (clozapine and olanzapine). Educate those identified to be at risk about the symptoms of diabetes.
- In all patients measure fasting glucose at baseline, at three months, and then annually. Repeat this pattern if the drug is changed. The frequency of monitoring may be increased if there are changes in fasting glucose or if risk factors change.

- In patients at high risk of developing diabetes consider monthly fasting blood glucose for the first three months and then check blood glucose three monthly for the first year followed by annually thereafter.

Patients with high baseline risk factors for diabetes should be prescribed an antipsychotic with lower risk of adverse metabolic effects where possible. In patients where adverse metabolic effects emerge, antipsychotic treatment should be reviewed and metabolic disturbances actively treated.

Reference

1. http://www.bpac.org.nz/magazine/2007/february/antipsychotics.asp

Cardiac risks associated with flecainide

Prescribers are reminded of the risk of inducing 1:1 atrioventricular conduction, with a consequent paradoxical increase in ventricular rate, when flecainide (Tambocor™) is used to treat atrial flutter. This reaction is more likely to occur with the use of intravenous flecainide. Consultation with a specialist prior to use of flecainide in emergency situations is recommended.

Flecainide is a class I anti-arrhythmic agent, indicated only in patients without structural heart disease for the prevention, rapid control, or short-term prophylaxis of supraventricular and ventricular arrhythmias. The specific indications are listed in the New Zealand Tambocor™ data sheet, available on the Medsafe website. Please note that flecainide is not recommended for use in patients with chronic atrial fibrillation.

As with other class I anti-arrhythmic agents, there have been reports of patients treated with flecainide for tachycardia due to atrial flutter who have developed a paradoxical increase in the ventricular rate. This increase has been attributed to the induction of 1:1 atrioventricular conduction following the slowing of the atrial rate. A paradoxical increase in the ventricular rate may also occur in patients with atrial fibrillation who receive flecainide. Concomitant negative chronotropic therapy such as digoxin or beta-blockers may lower the risk of this complication, however the additive negative inotropic effects of flecainide and beta-blockers would suggest that this combination should be used under specialist supervision.

This is a timely reminder to consider the potential risk of cardiac adverse events associated with the use of flecainide. The New Zealand data sheet for Tambocor™ has recently been updated with further information regarding the cardiovascular and pro-arrhythmic adverse effects associated with flecainide.

The cough and cold season is on its way – caution for patients receiving SSRIs

Prescribers are reminded of the potential interaction between selective serotonin reuptake inhibitors (SSRI) and dextromethorphan, commonly included in cough and cold products. CARM has received a report of a patient taking citalopram who experienced a serotonin syndrome-type reaction following the use of an over the counter medicine containing dextromethorphan.

Serotonin syndrome is a dose-dependent toxic state caused by excess serotonin within the CNS and is characterised by mental, autonomic and neuromuscular changes. Clinical features include confusion, agitation, hyperactivity sweating, tachycardia, ataxia, hypertonia and tremor.

The mechanism for this interaction is not fully understood; however it has been suggested that the reaction may be due to the additive effects of SSRIs and dextromethorphan on serotonin transmission. SSRIs are known to inhibit cytochrome P450 isoenzyme CYP2D6, the same enzyme which catalyses dextromethorphan metabolism.[1]

Patients should be informed about this potentially serious drug interaction and advised to check with their pharmacist when purchasing cough and cold medicines. Pharmacists are reminded to ask about concommitant medicines when recommending cough and cold products.

Reference

1. SSRIs and related antidepressants. In Stockley IH (Ed) *Stockley's Drug Interactions* Electronic version, 2009.

Medicines interaction reports – NSAIDS

Recent reports of serious adverse reactions with NSAIDs have highlighted the importance of questioning patients about their use of over the counter medicines (OTC).

CARM has identified four reports of serious adverse reactions to NSAIDs including: gastrointestinal bleed (requiring transfusion); gastric, duodenal and colonic ulcers; acute renal failure; and haematemesis. All four reports were in patients who had taken OTC ibuprofen in addition to prescribed diclofenac or, in patients who had taken excessive doses of OTC ibuprofen for extended periods.

These reports indicated that patients did not read the dosing recommendations or the risks in taking other medicines provided with these products. Prescribers are reminded to advise patients about their use of OTC medicines when prescribing NSAIDS.

Corticosteroids and avascular necrosis

CARM has received a number of reports of avascular necrosis (AVN) in association with corticosteroid use. The reports describe the involvement of major joints such as hips, knees and ankles, often with bilateral involvement. International reports have also included other joints, including the shoulder and wrists. AVN usually causes significant chronic pain and reduced mobility, with some patients requiring joint replacements.

The pathogenesis of AVN is not yet fully understood, but may involve steroid induced osteoblast apoptosis.

The CARM reports involve patients who were prescribed corticosteroids for asthma, immunosuppression in transplant recipients, polymyalgia rheumatica, rheumatoid arthritis, eczema, and cerebral oedema. International reports of AVN have included an association with the use of pulse steroid therapy in multiple sclerosis.

AVN usually occurs with high doses of corticosteroids over a period of a few weeks to several years. Other known risk factors for AVN include: alcoholism, infections, hyperbaric events, storage disorders, marrow infiltrating diseases, coagulation defects, sickle cell anaemia and some autoimmune diseases.

As some patients who develop AVN remain asymptomatic, the severity of symptoms cannot be taken as a guide to the severity or stage of AVN.

As the clinical outcome is dependent on the stage at which diagnosis of AVN is made, prescribers should be alert to symptoms of joint pain in patients using corticosteroids and are advised to investigate these symptoms early. In the presence of a confirmed diagnosis of AVN, stopping or interrupting corticosteroid treatment should be considered. Prescribers should also consider investigating for further conditions associated with AVN such as, myeloproliferative diseases, coagulation disorders, and autoimmune conditions.

Reference

1. Assouline-Dayan Y. Chang C. Greenspan A. Schoenfeld Y. Gershwin ME. (2002), Pathogenesis and natural history of osteonecrosis. *Seminars in Arthritis and Rheumatism*, 32(2): 94 – 124.

Complementary Medicine Corner – Risk of myalgia with red yeast rice extract

Prescribers are reminded that complementary medicines can contain pharmacologically active ingredients that may cause adverse reactions or interact with conventional medicines.

CARM has received a report of chest pain, myalgia, elevated creatine kinase levels, and abnormal liver function tests in an individual who had taken a combination of red yeast rice extract, saw palmetto (*Serenoa repens*), coenzyme Q_{10} and multivitamins. Red yeast rice extract is an extract of red yeast (*Monascus pupureas*) grown on rice. It contains the constituent lovastatin, a naturally-occurring statin with a similar adverse reaction profile to other statins that are approved medicines in New Zealand. Lovastatin can cause severe muscle problems (myalgia) leading to kidney impairment.[1] The risk of myalgia is increased in patients taking other medicines such as itraconazole, ketoconazole, and other statins.

Prescribers are reminded to ask their patients about their use of complementary medicines, and report any suspected adverse reactions to CARM.

Reference

1. FDA – MedWatch (2007) FDA Warns Consumers to Avoid Using Red Yeast Rice Products.

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.

Regular amendments to the list of reactions are made either in response to adverse events reported in New Zealand or international pharmacovigilance issues.

Please report **all cases** of the following adverse reactions to: CARM, NZ Pharmacovigilance Centre, PO Box 913, Dunedin 9054. Use the reporting form provided with each edition of *MIMS New Ethicals*, 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* references
Complementary and alternative medicines*	all adverse reactions	Vol.30(1), February 2009 & Vol.28(1), November 2007 & Vol.23(2), July 2002
Leflunomide	all adverse reactions	Vol.29(1), June 2008 & Vol.27(1), June 2006 & Vol.26(2), December 2005 & Vol.25(1), May 2004
Pioglitazone and Rosiglitazone	all adverse reactions	Vol.29(1), June 2008 & Vol.28(1), November 2007 & 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 medicine currently being monitored is: **Varenicline (Champix)**

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 9054. Use the reporting form, provided with each edition of *MIMS New Ethicals* or download it from either the NZ Pharmacovigilance Centre or Medsafe websites: 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 9054).

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Medsafe: New Zealand Medicines and Medical Devices Safety Authority
A business unit of the Ministry of Health.

Editor: Chris James
Medsafe, PO Box 5013, Wellington 6145, New Zealand
Ph: (04) 819 6800 Fax: (04) 819 6806
E-mail: chris_james@moh.govt.nz

Editorial Team:

Joanne Hart	Manager Clinical Risk Management
Kevin Sheehy	Senior Medical Advisor
Jan McNee	Advisor Pharmacovigilance
Abby Cutfield	Advisor Pharmacovigilance
Susan Kenyon	Senior Advisor Pharmacovigilance

Group Manager: Stewart Jessamine

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