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Antithrombotic Medicines – Still Causing Bleeding

Anticoagulants and antiplatelet agents (antithrombotics) are widely used to treat a number of conditions, with recent guidance on their use being issued by the Best Practice Advocacy Centre (BPAC)[1].

Bleeding is the major risk associated with all antithrombotics. The Centre for Adverse Reaction Monitoring (CARM) continues to receive reports of serious bleeds experienced by patients taking these medicines.

An overview of 12 months of reporting to CARM is shown in Table 1. The main sites of serious bleeding were most often gastrointestinal or intracranial in origin.

Only a small fraction of suspected adverse reactions are reported to CARM, nevertheless these reports show that serious bleeds do occur with antithrombotics and that some bleeds may have been preventable. For example, although combination therapy is recommended for some conditions, adverse reaction data continues to indicate a major risk factor for bleeding is the concomitant use of more than one antithrombotic medicine.

Early treatment of bleeds is desirable and patients and/or carers should be advised to monitor for early signs of bleeding.

Key Messages

- A major risk factor for bleeds is the use of more than one antithrombotic medicine.
- Patients and/or carers should be advised to monitor for the early signs of bleeding.

References

1. A New Zealand Consensus Forum. 2011. The use of antithrombotic medicines in general practice: a consensus statement. *Best Practice Journal*, 39: 10-21

Preventing Medication Errors: Tacrolimus Case Study

New formulations of existing medicines can sometimes cause confusion, especially when there is a change to dosing frequency.

This article draws prescribers' attention to the new prolonged-release formulation of tacrolimus that is now approved for use in New Zealand.

Table 1: Antithrombotic CARM reports associated with bleeding from 1 Oct 2010 to 30 Sept 2011.

Medicine	Total number of reports	Number of reports of bleeding (%)	Number of bleeding cases reported to be exposed to another anticoagulant or antiplatelet agent (%)	Number of bleeding cases reported to also be exposed to a NSAID or SSRI (%)
Aspirin	28	68	53	42
Clopidogrel	9	67	100	16
Dabigatran*	212	42	59	3
Dipyridamole	3	67	100	50
Enoxaparin	14	50	57	0
Rivaroxaban	3	0	N/A	N/A
Warfarin	32	56	50	11

* Dabigatran has been recently introduced with rapid uptake

Tacrolimus is currently marketed as Prograf and the new formulation as Prograf XL. Importantly, tacrolimus has a narrow therapeutic index and medication errors have the potential to significantly harm patients.

Prograf

- Is an **immediate release** formulation intended for **twice daily** dosing.

Prograf **XL**

- Is a **prolonged release** formulation intended for **once daily** dosing.

The manufacturer of Prograf and Prograf XL has employed a number of methods to reduce the risk of confusion between the two brands, such as:

- colour coding of the capsules and blisters, with distinctive colouring for immediate versus prolonged release capsules
- the use of packing overwrap to highlight the XL formulation and patient dosing cards
- the use of shelf talkers for pharmacies to reduce the potential for picking errors.

In addition, the manufacturer is attempting to introduce warning flags on prescribing and dispensing software.

International experience

Cases of medication errors, due to confusion over tacrolimus formulations, have already been reported in other countries. In some cases, these errors resulted in serious adverse reactions, including rejection of transplanted organs[1].

Errors have occurred at the prescribing, dispensing and administration of tacrolimus.

References

1. Medicines and Healthcare Products Regulatory Agency. 2010. Oral tacrolimus products: measures to reduce risk of medication errors. *Drug Safety Update*, 3(10): 5

Key Messages

- To reduce the potential for error, tacrolimus should be prescribed with a full description of the drug, the formulation (immediate release or prolonged release), the strength and frequency of dosing.
- Prescribers should also consider adding the brand name to prescriptions.
- Pharmacists should contact the prescriber if the strength, brand or formulation is not absolutely clear.
- Switching between formulations or brands of tacrolimus requires careful medical supervision and may require therapeutic monitoring and re-titration.
- Patients should be advised to familiarise themselves with the name and appearance of their tacrolimus medication and check with their doctor or pharmacist if they have any concerns about the medicine they receive.

Nicobrevin – Do the Benefits Outweigh the Risks?

Following the withdrawal of Nicobrevin in the United Kingdom, Medsafe requested a review of the benefits and risks of this medicine from the product sponsor. The Medicines Adverse Reaction Committee (MARC) reviewed this information along with information about the individual ingredients contained in Nicobrevin.

Nicobrevin is used as an aid to quitting smoking and contains: menthyl valerate, camphor, quinine and eucalyptus oil. These ingredients are claimed to help to relieve the symptoms associated with stopping smoking.

The MARC considered that studies reviewed in support of the efficacy of Nicobrevin provided little evidence of benefit. Studies reviewed included the Dankwa et al. study conducted in 92 smokers in 1988 and a recently updated Cochrane review[1,2].

However, despite the paucity of evidence of efficacy in the scientific literature, the MARC noted that even if this product only had a placebo effect this might still be helpful in enabling smokers to quit.

There was little evidence of frequent serious harm occurring with the use of Nicobrevin, although the following was noted:

- valerian may impair driving ability; this risk extends to all products containing valerian[3]
- valerian can cause gastrointestinal reactions[3]
- quinine, even at a low dose, can cause thrombocytopenia and hypersensitivity reactions in rare cases; this risk also extends to tonic water[4,5].

The MARC concluded that there was insufficient evidence demonstrating serious harm to justify removing the product from the New Zealand market.

To provide more information for patients and minimise the risk of adverse effects, the MARC recommended that the Nicobrevin package label and package insert be updated to reflect the risk of adverse reactions. Medsafe is working with the sponsor to update the label.

References

1. Dankwa E, Perry L, Perkins A. 1988. A double-blind, placebo-controlled study to determine the efficacy of Nicobrevin anti-smoking capsules. *British Journal of Clinical Practice*, 42(9): 359-363.
2. Stead LF, Lancaster T. 2006. Nicobrevin for smoking cessation. *Cochrane Database of Systematic Reviews*, Issue 2, Art. No. CD005990. DOI: 10.1002/14651858.CD005990.
3. European Medicines Agency. 2006. Community herbal monograph on *Valeriana officinalis* L., radix. Doc. ref. EMEA/HMPC/340719/2005. URL: **www.ema.europa.eu/docs/en_GB/document_library/Herbal_-_Community_herbal_monograph/2009/12/WC500017925.pdf**
4. Brasic JR. 2001. Quinine-induced thrombocytopenia in a 64-year-old man who consumed tonic water to relieve nocturnal leg cramps. *Mayo Clinic Proceedings*, 76(8): 863-864
5. Bel B, Jeudy G, Bouilly D, et al. 2009. Fixed eruption due to quinine contained in tonic water: positive patch testing. *Contact Dermatitis*, 61(4): 242-244

Citalopram and Escitalopram – Similar Risk of QT Prolongation?

Citalopram and Escitalopram are selective serotonin reuptake inhibitors (SSRIs) used for the treatment of depressive illness.

A recent clinical study found that citalopram is associated with a dose dependent increase in the risk of QT prolongation[1]. QT prolongation is an established side effect of Class I and Class III antiarrhythmic medicines and a rare side effect of a wide range of other medicines that lead to cardiac dysrhythmia. For more information about drug-induced QT prolongation refer to the article published in the December 2010 edition of *Prescriber Update*[2].

The New Zealand data sheets for citalopram have been updated to describe the risk of QT prolongation, contraindicate its use in patients with congenital long QT syndrome and recommend a new maximum dose of 40 mg daily. Information on prescribing citalopram safely has recently been published by the Best Practice Advocacy Centre (BPAC)[3].

To assess if this risk extended to escitalopram, a second clinical study was conducted[4]. The study determined that escitalopram was associated with substantially less QT prolongation than citalopram and was only seen at supratherapeutic doses (30 mg daily). In New Zealand the recommended dose is 10 mg once daily, which can be increased to a maximum of 20 mg daily depending on the patient's response[4-6].

Although other SSRIs are available in New Zealand, the relative risk of QT prolongation associated with the use of these medicines is not yet clearly defined. Medsafe is in the process of reviewing this risk for all SSRIs and will provide further information when it is available.

Prescribers are reminded to consider the risks and benefits of SSRI treatment, particularly before prescribing in patients with congenital long QT syndrome or those with multiple risk factors.

Prescribers are advised to seek specialist cardiological and/or psychiatric advice if necessary.

Key Messages

- Citalopram is associated with a risk of QT prolongation at therapeutic doses.
- Escitalopram is associated with an increased risk of QT prolongation at supratherapeutic doses.
- Citalopram and escitalopram should be used with caution in patients with multiple risk factors for QT prolongation.

References

1. Food and Drug Administration. 2011. Abnormal heart rhythms associated with high doses of Celexa (citalopram hydrobromide). *Drug Safety Communication*, 24 August 2011
2. Medsafe. 2010. Drug-induced QT prolongation and Torsades de Pointes – the facts. *Prescriber Update*, 31(4): 27-29
3. Best Practice Advocacy Centre. 2012. Prescribing citalopram safely: an update. *Best Practice Journal*, 42: 38-41
4. Healthcare Logistics. 2011. *Lexapro data sheet*
5. Mylan New Zealand Ltd. 2011. *Loxalate data sheet*
6. Apotex NZ Ltd. 2011. *Apo-Escitalopram data sheet*

Aqueous Cream – Moisturiser or Irritant?

Aqueous cream is the most widely prescribed emollient for the treatment of dry skin conditions and is often the first line of treatment for patients with eczema[1]. However, recent studies suggest that the use of aqueous cream can damage the skin barrier when used as a leave-on emollient[1-3].

Aqueous cream BP first appeared in the British Pharmacopoeia in 1958 and the formulation has remained unchanged since then. One of its ingredients, sodium lauryl sulphate, is an emulsifier and known skin irritant. Although the product was originally intended to be a wash product, it is now generally prescribed and used as both a soap substitute and leave-on emollient[1].

Users of aqueous cream have reported high rates of skin irritation, prompting the National Institute for Health and Clinical Excellence (NICE) in the United Kingdom to remove it from their guideline on the management of eczema in 2007.

Eczema arises from a combination of genetic and environmental factors leading to the breakdown of the skin barrier. Soap and surfactants, such as sodium lauryl sulphate, have been identified as negative environmental factors and their use is not recommended in patients with eczema.

New research, published in the *British Journal of Dermatology*, shows that aqueous cream induces skin irritation[2]. The study compared parameters of skin barrier function between skin treated with aqueous cream as a leave-on emollient and untreated skin. Treated areas showed a decrease in the size and maturity of keratinocytes, causing the skin's protective structure to be compromised. Treated skin also showed increased transepidermal water loss, reflecting impaired barrier function.

In patients with a history of atopic dermatitis aqueous cream appeared to cause a greater amount of skin barrier damage and subjective irritation was common[3].

These papers highlight the importance of not using products containing sodium lauryl sulphate, such as aqueous cream, as leave-on emollients as they may act to exacerbate skin damage rather than support skin barrier function.

References

1. Tang M, Guy RH. 2010. Effect of Aqueous Cream BP on human stratum corneum *in vivo*. *British Journal of Dermatology*, 163(5): 954-958
2. Mohammed D, Matts PJ, Hadgraft J, et al. 2011. Influence of Aqueous Cream BP on corneocyte size, maturity, skin protease activity, protein content and transepidermal water loss. *British Journal of Dermatology*, 164(6): 1304-1310
3. Danby SG, Al-Enezi T, Sultan A, et al. 2011. The effect of aqueous cream BP on the skin barrier in volunteers with a previous history of atopic dermatitis. *British Journal of Dermatology*, 165(2): 329-334

Complementary Corner: St John's Wort and Serotonin Syndrome

A single cup of Healtheries "Be Happy" tea and two days of citalopram treatment has been associated with a case of serotonin syndrome resulting in hospitalisation.

The report received by the Centre for Adverse Reactions Monitoring (CARM) describes a patient who was started on low dose citalopram one day after ingesting "Be Happy" tea. After just two doses of citalopram, the patient developed symptoms consistent with moderate serotonin syndrome[1].

"Be Happy" tea lists 820 mg of St John's Wort per tea bag.

St John's wort is a herbal substance from the plant St John's wort (*Hypericum perforatum*). St John's wort is traditionally used for the treatment of depression and related conditions such as anxiety, tiredness, loss of appetite and trouble sleeping.

St John's wort is known to interact with selective serotonin reuptake inhibitors (SSRIs), in the same way as serotonergic drugs such as tramadol and citalopram, by further increasing the serotonin level in the brain[2]. The concomitant use of St John's wort and SSRIs is not recommended and is included as an interaction in SSRI data sheets[2].

Adverse reactions from interactions with other medicines could happen with any product that contains a large amount *H. perforatum*. Further information about clinically important interactions of St John's wort can be found in the February 2001 edition of *Prescriber Update*[3].

Healthcare professionals are encouraged to ask patients about their use of complementary and alternative medicines and to report all suspected adverse reactions to CARM.

References

1. Medsafe. 2010. Serotonin syndrome/toxicity - reminder. *Prescriber Update*, 31(4): 30-31
2. European Medicines Agency. 2009. Community herbal monograph on *Hypericum perforatum* L., herba (well-established medicinal use). Doc. Ref. EMA/HMPC/101304/2008. URL: **www.emea.europa.eu/docs/en_GB/document_library/Herbal_-_Community_herbal_monograph/2010/01/WC500059145.pdf**
3. Medsafe. 2001. Interactions with St John's wort (*Hypericum perforatum*) preparations. *Prescriber Update*, 20: 42-48

Seasonal Flu Vaccine – Spontaneous Reporting in 2011

The Centre for Adverse Reactions Monitoring (CARM) and Medsafe thank everyone who contributed to the monitoring of the flu vaccine last season by reporting suspected adverse reactions.

In 2011, approximately 200 reports of adverse events suspected to be related to influenza vaccination were received by CARM. This compares with over 400 reports received in 2010, when concerns were raised about cases of fevers and febrile convulsions in children.

The funded vaccines in 2011 were Fluvax and Fluarix. Fluarix was recommended by the Ministry of Health for eligible children under nine years of age.

Use in Children

In 2011, there was only one report of febrile convulsions suspected to be associated with influenza vaccine (Vaxigrip). There were four reports of death coincident with influenza immunisation in 2011. CARM did not consider any of these reports to be caused by the vaccine.

Fever was reported in nine children, including one child less than nine years of age who received Fluvax. There was one report of an almost immediate allergic reaction (including urticaria and periorbital oedema). The child was appropriately treated and recovered without sequelae.

Guillain-Barré Syndrome

There were two instances of patients in their 70's experiencing Guillain-Barré syndrome following immunisation. However, information about possible confounding factors, such as prior infections, was not provided.

Epidemiological studies have not consistently found an association between Guillain-Barré syndrome and influenza vaccines, with the reporting rate for these events remaining lower than the background rate in the general population[1-3].

Conclusions

After an analysis of reports received in New Zealand in 2011, CARM considered the nature of reports was as expected for vaccine related adverse events.

Next Season

The strains of influenza to be used in next season's (2012) vaccine will remain unchanged, as do the PHARMAC funded brands (Fluvax and Fluarix). For eligible children under nine years of age, Fluarix continues to be the recommended influenza vaccine.

References

1. Haber P, Sejvar J, Mikaeloff Y, et al. 2009. Vaccines and Guillain-Barré syndrome. *Drug Safety*, 32(4): 309-323
2. Stowe J, Andrews N, Wise L, et al. 2006. Bell's palsy and parenteral inactivated influenza vaccine. *Human Vaccines*, 2(3): 110-112
3. Black S, Eskola J, Siegrist CA, et al. 2009. Importance of background rates of disease in assessment of vaccine safety during mass immunisation with pandemic H1N1 influenza vaccines. *Lancet*, 374(9707): 2115-2122

Reminder: Depression and Suicidality Can Occur With Interferon Use

Prescribers are reminded that depression and/or suicidal ideation are commonly reported side effects of interferon alpha therapy and have also been reported with interferon beta use[1,2].

Prescribers should also be aware that patients with chronic hepatitis C infection and multiple sclerosis (MS) have a high background risk of psychiatric disorders such as depression.

Interferons are naturally occurring cytokines with antiviral and immunomodulatory properties. The three major interferon classes (alpha, beta and gamma) have overlapping but distinct biological activities.

Interferon alpha is indicated for the treatment of chronic hepatitis B and C infection, haematological malignancies (e.g. hairy cell leukaemia, chronic myelogenous leukemia, multiple myeloma and non-Hodgkin's lymphoma) and Kaposi's sarcoma. Interferon beta is indicated for the treatment of MS.

The Centre for Adverse Reaction Monitoring (CARM) has received six reports of suicidal ideation/tendency and three reports of death by suicide, associated with the use of interferon alpha. This includes three patients taking pegylated interferon plus ribavirin.

Indications for use were hepatitis C (5), chronic myelogenous leukemia (1) and unknown (3). The duration to onset of symptoms ranged from two weeks to 11 months (average 4.8 months). Of the nine patients, five patients had other risk factors for suicidal ideation including hepatitis C infection (5), intravenous drug use (1) concomitant ribavirin (2) and co-existing depression (4).

Possible activation symptoms (e.g. agitation, anxiety, aggression and irritability) were also experienced by six patients. The extent of additional psychosocial factors was not reported.

CARM has also received one report of suicidal ideation with interferon beta (in a patient with MS).

Key Advice for Healthcare Professionals[1,3]

- Patients should be screened for psychiatric symptoms prior to interferon treatment.
- Interferon should be used with caution and psychiatric review should be considered in patients with current depression or a history of depression.
- Mood and suicidal ideation should be monitored closely during interferon therapy.
- Patients should be advised to seek medical advice immediately if symptoms of depression or suicidal ideation occur or worsen during interferon treatment.
- Specialist advice should be sought if depression and/or suicidal ideation do not improve with treatment. The potential benefit of ongoing interferon treatment should be weighed carefully against the risks of worsening depression.

References

1. Sockalingam S, Links PS, Abbey SE. 2011. Suicide risk in hepatitis C and during interferon-alpha therapy: a review and clinical update. *Journal of Viral Hepatitis*, 18(3): 153-160
2. Goeb JL, Even C, Nicolas G, et al. 2006. Psychiatric side effects of interferon-beta in multiple sclerosis. *European Psychiatry*, 21(3): 186-193
3. Roche Products (New Zealand) Limited. 2011. *Pegasys data sheet*

Note: *PHARMAC fully subsidises interferon alpha (Pegasys, Pegasys RBV, Intron A and Roferon A) under special authority for the treatment of chronic hepatitis B and C infection and interferon beta (Avonex and Betaferon) for the treatment of MS.*

Adverse Reaction Reporting in New Zealand in 2011

All medicines have risks and benefits.

Before a medicine is released into the New Zealand market, safety and efficacy experience is limited to its use in clinical trials. Some important reactions may not be observed until a large number of people have received the medicine or have taken the medicine for a long period. Continued monitoring of adverse reactions is therefore essential.

National adverse reactions reporting activities (spontaneous reporting) in New Zealand are coordinated by Medsafe and the Centre for Adverse Reactions Monitoring (CARM).

Healthcare professionals (and consumers) can report a suspected adverse reaction to medicines (including vaccines) and complementary therapies (CAMs) by submitting a report through one of the following methods:

1. completing a yellow card sent via freepost to CARM
2. downloading a form from either the CARM or Medsafe websites
3. completing an online report available from either the CARM or Medsafe websites
4. electronic reporting through GP software
5. *Prescriber Update* form
6. iPhone app.

These reports are subsequently analysed to identify possible safety signals that require further investigation. Possible safety signals may appear on the M² scheme (**medsafe.govt.nz/profs/M2MedicinesMonitoring.asp**) and/or further action may be taken. Information about pharmacovigilance in New Zealand is available at **www.medsafe.govt.nz/Consumers/Safety-of-Medicines/Medicines-Safety-and-Pharmacovigilance.asp**.

In 2011, CARM received a total of 4331 suspected adverse reaction reports. This number includes suspected adverse reactions to medicines, vaccines and CAMs. The number of reports submitted has remained consistent for the past four years (Figure 1).

The majority of the reports received by CARM in 2011 were associated with medicines (66.5%) (Figure 2). Vaccines contributed to 33.1% of total suspected adverse reports, with CAMs making up the remaining 0.4%. This is a similar breakdown when compared to the reports received in 2010 (Figure 2).

Reports to CAMs remain low with only 19 submitted in 2011. Possible factors that could explain the low numbers of reports include: adverse reactions to CAMs are rare, adverse reactions to CAMs are not well recognised or a lack of awareness that adverse reactions to CAMs can be reported to CARM.

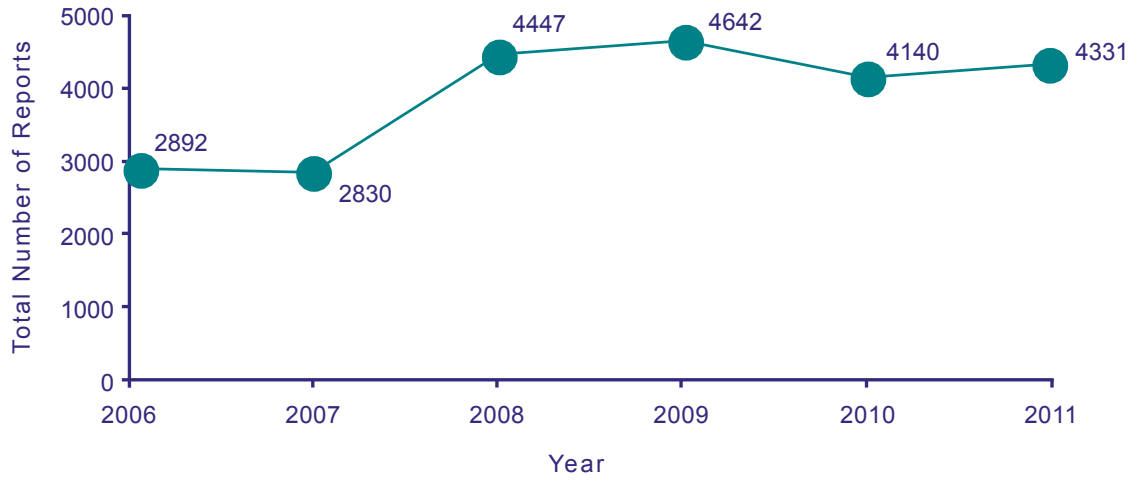

Figure 1: Adverse reaction reports submitted to CARM from 2006 to 2011.

Figure 2: Types of adverse reaction reports from 2006 to 2011.

Examination of the suspected adverse reaction reports received in 2011 showed 21.7% of total reports were considered to be serious. A serious adverse reaction is determined by CARM according to internationally agreed criteria i.e. resulting in hospitalisation, life-threatening, fatal, results in a disability, requires intervention to prevent permanent disability or results in a congenital abnormality.

Approximately one third of reports relating to medicines were considered serious and 10.5% of CAM reports received by CARM were considered serious (Table 1). Interestingly, only 4.3% of vaccine reports submitted were deemed serious.

The source of adverse reaction reports received in 2011 is shown in Figure 3. In 2011, the majority of adverse reaction reports submitted by healthcare professionals came from nurses, followed by GPs then hospital doctors (Figure 3).

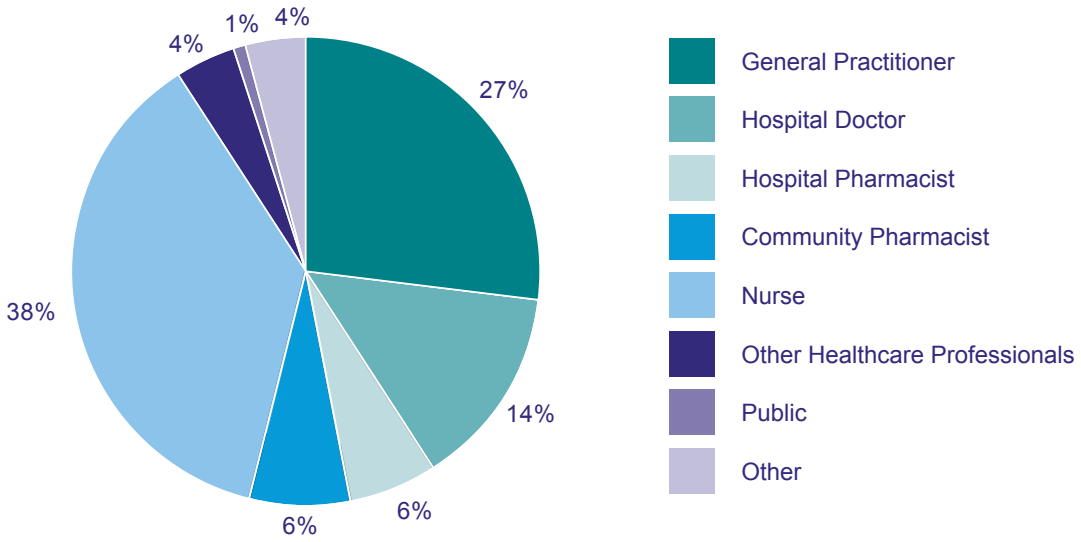

Figure 3: Source of adverse reaction reports from Healthcare Professional in New Zealand in 2011.

Table 1: Types of adverse reactions reports for 2011.

Type	Serious (%)	Non-serious (%)
Medicines	30.5	69.5
Vaccines	4.3	95.7
CAMs	10.5	89.5

Medsafe and CARM would like to thank all those who have contributed to pharmacovigilance in New Zealand by submitting reports of suspected adverse reactions and encourage continued support for 2012.

Adverse reaction reporting provides valuable information about the use of medicines in clinical practice and is a vital part of pharmacovigilance in New Zealand.

Further information about adverse reactions and how to submit an adverse reaction report can be found on the Medsafe website, **www.medsafe.govt.nz**, or on the CARM website, **www.otago.ac.nz/carm.**

IMMP Update: Varenicline (Champix) Monitoring

The varenicline post-market monitoring project was contracted by Medsafe to the Intensive Medicines Monitoring Programme (IMMP).

Since monitoring began in 2007, the varenicline patient cohort has now reached its pre-specified cohort size and now contains over 12,000 patients.

A number of important interim findings have been published based on data from the IMMP including:

- information about the utilization of varenicline in New Zealand, including identification that some patients were not receiving the recommended 12 weeks of treatment[1]
- analyses of the frequency of psychiatric adverse events[2,3]
- a case series of cardiovascular events in patients taking varenicline[4]
- a case series of patients describing epistaxis and other bleeding events while taking this medicine[5].

Final analysis of the varenicline data collected in this monitoring project is expected in mid-2012 and will be summarised in a future edition of *Prescriber Update*.

The IMMP has informed Medsafe that varenicline questionnaires will continue to be sent out after 30 June 2012. Please continue to return any outstanding questionnaires to the IMMP in the usual way.

Thank you to all healthcare professionals who have participated in this monitoring project and have provided valuable information about the safety and use of varenicline.

IMMP methodology can be used to investigate many different medicine safety issues. Organisations are able to contract IMMP studies to answer their research questions.

Healthcare professionals will be alerted to any new post-market monitoring projects as they are identified and initiated.

References

1. Harrison-Woolrych ML, Ashton J. 2010. Utilization of the smoking cessation medicine varenicline: an intensive post-marketing study in New Zealand. *Pharmacoepidemiology and Drug Safety*, 19(9): 949-953
2. Harrison-Woolrych ML. 2009. Varenicline and suicide: safety data from New Zealand. *British Medical Journal*, 339: b5654. DOI: 10.1136/bmj.b5654
3. Harrison-Woolrych ML, Ashton J. 2011. Psychiatric adverse events associated with varenicline: an intensive post marketing prospective cohort study in New Zealand. *Drug Safety*, 34(9): 763-772.
4. Harrison-Woolrych ML, Maggo S, Tan M, et al. 2012. Cardiovascular events in patients taking varenicline: a case series from intensive postmarketing surveillance in New Zealand. *Drug Safety*, 35(1): 33-43
5. Harrison-Woolrych ML, Harmark L, Tan M, et al. 2012. Epistaxis and other haemorrhagic events associated with the smoking cessation medicine varenicline: a case series from two national pharmacovigilance centres. *European Journal of Clinical Pharmacology*. DOI: 10.1007/s00228-012-1220-y.

MARC's Remarks: December Meeting

The Medicines Adverse Reactions Committee (MARC) met on 8 December 2011 and made the following recommendations.

The MARC was provided with an update on the safety profile of **dabigatran** (Praxada). The Committee was advised that, compared with the first few weeks of funding, only two reports of medication error were received by the Centre of Adverse Reaction Monitoring (CARM) in October. The MARC were satisfied that the number of medication errors associated with dabigatran treatment is decreasing and agreed that the balance of benefits and risks remains positive at present.

The MARC reviewed the benefits and risks of **Nicobrevin** following its withdrawal from the United Kingdom. Refer to the article in this edition of the *Prescriber Update*[1].

The MARC was provided with a comparison of usage data and spontaneous reports involving **tramadol** before and one year following funding of Arrow-Tramadol 50 mg capsules by PHARMAC. The Committee acknowledged that the adverse event reports received since tramadol was funded have been similar in nature and proportion to those received prior to funding.

Further information relating to these matters is available from the MARC meeting minutes published on the Medsafe website:

www.medsafe.govt.nz/profs/adverse/Minutes148.htm

References

1. Medsafe. 2012. Nicobrevin – benefit risk review. *Prescriber Update*, 33(1): 2-3

WE NEED YOUR HELP!

M² MEDICINES MONITORING

Please send your reports for these potential safety issues* listed in the table below.

Medicine	Potential safety issue	Active monitoring ends
ENDING SOON Lansoprazole, Pantoprazole	Hypomagnesaemia	31 March 2012
EXTENDED Sildenafil	Thromboembolism	30 September 2012
NEW Cetirizine	Severe Mood Disorder	30 September 2012

- The M² scheme does not replace routine adverse reaction reporting. Find out how to report at: **http://www.otago.ac.nz/carm** or **http://www.medsafe.govt.nz**

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* The appearance of a possible safety issue in this scheme does not mean Medsafe and CARM have concluded that this medicine causes the reaction.

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