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MANATŪ HAUORA

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Codeine and breastfeeding

Healthcare professionals are reminded that codeine use by breastfeeding mothers has been associated with fatal cases of infant morphine toxicity. Healthcare professionals should carefully consider the risks and benefits of codeine before recommending its use to breastfeeding mothers.

The labels for over-the-counter (OTC) products containing codeine have recently been updated to advise against codeine use in breastfeeding except on medical advice. The doses of codeine available in some OTC preparations are considered sufficient to cause morphine toxicity in breastfed infants.

The *Lancet* published a case report in 2006[1] of an otherwise healthy 13 day old breastfed baby who died of morphine toxicity after his mother had been prescribed codeine (60mg twice daily for 2 days and then 30mg twice daily thereafter) to treat episiotomy pain. The baby experienced feeding difficulties and lethargy at day 7 and was found dead on day 13. Analyses of the baby's blood and the mother's breast milk found toxic levels of morphine in both. Genetic testing of the mother determined that she was an ultra-rapid metaboliser (URM) of codeine, leading to an increase in the rate and extent of conversion of codeine to morphine.

The prevalence of URM of codeine varies among different racial groups.[2] It is estimated that 1-10% of Caucasians are URMs; although it is unknown what proportion of Maori or Pacific people are affected. In the absence of genetic testing, it is not possible to identify URMs prior to prescribing codeine.

Patients should be advised of the symptoms of morphine toxicity in themselves (nausea, vomiting, somnolence, constipation and/or difficulty caring for the baby) and their baby (increased sleepiness, difficulty breastfeeding, breathing difficulties or limpness). Patients should be advised to discontinue codeine and to seek medical attention immediately if these symptoms occur.

References

1. Koren G, et al (2006). Pharmacogenetics of morphine poisoning in a breastfed neonate of a codeine-prescribed mother. *Lancet* 368:704.
2. FDA Public Health Advisory: Use of codeine by some breastfeeding mothers may lead to life-threatening side effects in nursing babies. August 2007. **http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm124889.htm**
3. PSM Healthcare Ltd t/a API Consumer Brands. 29 August 2007. Codeine Phosphate data sheet. **www.medsafe.govt.nz/profs/Datasheet/dsform.asp**

Withdrawal of sibutramine (Reductil) in New Zealand

The consent to distribute sibutramine containing medicines was formally revoked in New Zealand on 14 October 2010.

The withdrawal of sibutramine followed the Medicines Adverse Reactions Committee (MARC) recommendation on its benefits and risks. The review was prompted by the release of preliminary results of the Sibutramine Cardiovascular Outcome Trial (SCOUT). Subjects treated with sibutramine in this study had an increased risk of non-fatal myocardial infarction and non-fatal stroke compared to those given placebo.

Although the SCOUT study recruited high risk subjects, commonly with pre-existing cardiovasular disease, the MARC considered that the benefits of sibutramine on weight loss were modest. In addition the safety data for patients eligible for sibutramine was not sufficiently reassuring.

Of particular concern to the MARC and Medsafe was the difficulty in identifying patients at high risk for cardiovascular events, especially obese patients who are at very high risk and or may have had silent events.

Medsafe has advised patients to stop taking Reductil and to talk to a healthcare professional about alternative weight loss measures and maintenance programmes. There are no known adverse effects from stopping sibutramine abruptly.

Further information on the withdrawal of sibutramine in New Zealand is available at: **www.medsafe.govt.nz/hot/media/2010/SibutramineOct2010.asp**

Sibutramine has also been withdrawn in Europe, the United States, Canada and Australia.

Drug-induced QT prolongation and Torsades de Pointes – the facts

Prescribers are advised to consider the possibility of drug-induced QT prolongation or Torsades de Pointes (TdP) in patients presenting with new onset syncope, palpitations, seizures or resuscitated cardiac arrest.

QT prolongation, a surrogate marker for the risk of developing TdP, is an established side effect of Class I and Class III anti-arrhythmic medicines. It is also a rare side effect of a wide range of non-cardiac medicines including some antibiotics, antihistamines, opioid analgesics and complementary medicines.

What is QT prolongation?

QT prolongation is a measure of delayed ventricular repolarisation. Excessive QT prolongation can predispose the myocardium to the development of early after-depolarisations, which in turn can trigger re-entrant tachycardias such as TdP.

Although the relationship between QT interval duration and the risk of TdP is not fully understood, a corrected QT interval (QT_C) of >500ms[1] or an increase in the QT_C of >60ms[2] is generally considered to confer a high risk of TdP in an individual patient.

Table 1: QT_C values for normal and prolonged QT interval after correction with Bazett's formula[3]

QTc values by Age and Sex (ms)			
	1-15 years (ms)	Adult males (ms)	Adult females (ms)
Normal	<440	<430	<450
Borderline	440-460	430-450	450-470
Prolonged (top 1%)	>460	>450	>470

QT_C = corrected QT interval which corrects for heart rate. It is often derived using Bazett's formula (QT_C = QT interval/√R-R interval), which can be unreliable at HR<50 bpm or >90 bpm.

What medicines cause QT prolongation/TdP?

An up-to-date database of medicines with the potential to cause QT prolongation/TdP, including a separate list of medicines to be avoided by patients with congenital long QT syndrome, is available on-line at **www.qtdrugs.org.**

The database, which is maintained by the Arizona Center for Education and Research on Therapeutics, groups medicines according to the level of evidence supporting an association with QT prolongation/ TdP (see Table 2 and Table 3 below).

Table 2: Examples of non-cardiac medicines that are generally accepted to have a risk of QT prolongation/TdP (see www.qtdrugs.org for a complete list)

Anti-infectives	Anti-emetics/gastric motility agents	Anti-psychotics	Opioid analgesics	Antihistamines
Clarithromycin Erythromycin Chloroquine Pentamidine	Domperidone Cisapride #	Haloperidol Chlorpromazine	Methadone	Terfenadine #

these medicines have been withdrawn worldwide due to risk of QT prolongation/TdP

Table 3: Examples of non-cardiac medicines that are possibly associated with a risk of QT prolongation/TdP (see www.qtdrugs.org for a complete list)

Anti-infectives	Anti-emetics	Antipsychotics	Antidepressants	Anti-cancer
Azithromycin Roxithromycin Telithromycin Moxifloxacin Amantadine	Ondansetron Dolasetron Granisetron	Risperidone Quetiapine Sertindole Ziprasidone Lithium Clozapine	Escitalopram Venlafaxine	Tamoxifen Nilotinib Lapatinib

What are the risk factors for drug induced QT prolongation/TdP?

The available evidence suggests that additional risk factors must be present before drug-induced QT prolongation/TdP will occur. In most reported cases at least one additional risk factor was present and in 70% of cases two risk factors were present.[1]

Most risk factors are continuous variables, for instance the risk from hypokalaemia increases as potassium levels fall.

Table 4: Risk factors for the development of drug induced QT prolongation/TdP [1,4,5,6,7]

Unmodifiable risk factors	Potentially modifiable risk factors
Female gender (present in 70% of cases)	Hypokalaemia or severe hypomagnesaemia
Increasing age	Absolute or relative bradycardia (including recent conversion from AF)
Genetic predisposition • Congenital long QT syndrome • Family history of sudden death • History of previous drug-induced QT prolongation	Drug interactions • Use of >1 QT prolonging medicine • Medicines that inhibit the metabolism of another QT prolonging medicine • Medicines that cause electrolyte abnormalities or may cause renal or hepatic dysfunction
Structural heart disease/LV dysfunction	Starvation or obesity
Impaired elimination due to renal or hepatic disease	High drug concentrations due to overdose or rapid IV administration

What should you do before prescribing a QT prolonging medicine?

- Screen for other risk factors for QT prolongation, including possible medicine interactions and electrolyte abnormalities. Correct any modifiable risk factors.
- Baseline ECGs should be performed in high risk patients, or in patients receiving more than one QT prolonging medicine. A non-QT prolonging medicine should be considered in these patients if possible.

- Do not prescribe a QT prolonging medicine to patients already receiving a Class I or Class III anti-arrhythmic medicine.
- Patients should be advised to avoid consuming grapefruit juice, liquorice or any complementary medicines in addition to a QT prolonging medicine.[8]

What monitoring should be undertaken?

- All patients should be advised to report symptoms of arrhythmia or any conditions that could lead to hypokalaemia or renal dysfunction.[9,10]
- ECGs should be performed in all patients with symptoms of arrhythmia and periodically in patients at high risk of QT prolongation/TdP.
- If there are risk factors for electrolyte disturbance, electrolytes should be measured periodically. Hypokalemia or hypomagnesaemia should be corrected.

What should you do if QT prolongation occurs?

- If QT prolongation (i.e. QT >500ms or an increase of >60ms) or symptomatic arrhythmia occurs, the medicine should be stopped unless there are compelling reasons to continue.
- Specialist advice from a cardiologist should be sought. Investigation for congenital long QT syndrome may be appropriate, particularly if the QT_C fails to normalise after the medicine is discontinued.

What should you do if TdP occurs? [9,11]

- Sustained episodes or unstable patients require DC cardioversion.
- Intravenous magnesium sulphate should be given immediately.
- The suspect medicine should be withdrawn and any electrolyte abnormalities corrected.
- Cardiac pacing or isoprenaline infusion should be considered for refractory cases.

References

1. Heist EK and Ruskin JN (2005). Drug-induced proarrythmia and use of QT_C prolonging agents: Clues for clinicians. *Heart Rhythm* 2(11):S1-S8.
2. Barnes BJ and Hollands J M (2010). Drug-induced arrhythmias. *Crit Care Med* 38(6 Suppl): S188-S197).
3. Yap YG and Camm AJ (2003). Drug induced QT prolongation and torsades de pointes. *Heart 89:1363-1372.*
4. Viskin S (1999). Long QT syndromes and torsades de pointes. *The Lancet 354; 1625-1633.*
5. Morissette P et al (2005). Drug induced long QT syndrome and torsade de pointes. *Canadian Journal of Cardiology* 21(10):857-864.
6. Al Khatib SM et al (2003). What Clinicians Should Know About the QT interval. *JAMA 289 (16): 2120-2127.*
7. Fraley MA et al (2005). Obesity and the electrocardiogram. *Obesity Reviews 6: 275-281.*
8. Personal communication. 18 November 2010. Cardiologist. Auckland.
9. Gowda RM et al (2004). Torsade de pointes: the clinical considerations. *International Journal of Cardiology* 96:1-6.
10. Roden DM (2005). Drug-Induced Prolongation of the QT interval. *NEJM* 350;10:1013-1022.
11. Zipes et al (2006). ACC/AHA/ESC Guidelines for Management of Patients With Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death. *Journal of the American College of Cardiology* 48(5)e247-e346.

Serotonin syndrome/toxicity – reminder

Serotonin syndrome, more correctly termed serotonin toxicity, is a set of predictable type A dose dependent adverse reactions caused by increased intra-synaptic/extracellular serotonin.[1]

Since serotonin toxicity can be fatal after a single dose of an inappropriate medicine (or combination) it is vitally important to be familiar with both the causal agents and signs and symptoms.

A number of diagnostic criteria have been suggested, the most commonly quoted are Sternbach's[2] (based on a review of 38 case reports) and the Hunter criteria (derived from Australian toxicology data).[3] The Hunter criteria are generally considered to be preferable as they are based on a larger sample size (2222 cases) and have been shown to be simpler, more sensitive and more specific.[4]

The Hunter criteria can be grouped into a triad of clinical features:

Neuromuscular effects	Autonomic effects	Mental state changes
Hyperreflexia	Tachycardia	Agitation
Clonus (spontaneous or inducible)	Hyperthermia (mild< 8.5°C, severe ≥ 38.5°C)	Hypomania
Myoclonus	Diaphoresis	Anxiety
Shivering	Flushing	Confusion
Tremor	Mydriasis	
Hypertonia/ rigidity		

The most robust diagnostic feature of serotonin toxicity is clonus (spontaneous, inducible or ocular) and this differentiates serotonin toxicity from other toxic drug states.[3]

The severity of serotonin toxicity can generally be classified as: mild, moderate or severe. Severe toxicity is characterised by rapidly increasing body temperature associated with muscle rigidity; this is a medical emergency. The patient may deteriorate to multiorgan failure and death without treatment. Recommended treatment is generally supportive. Serotonin receptor antagonists such as chlorpromazine and cyproheptadine have been used to treat serotonin toxicity; sedation, muscle paralysis and ventilation may be required in severe cases. Although cases of moderate toxicity are unlikely to be fatal, symptoms can cause significant distress to the patient and supportive treatment should be provided.[3]

The three pharmacological mechanisms contributing to serotonin toxicity are: serotonin reuptake inhibition (SRI), presynaptic serotonin release and monoamine oxidase (MAO) inhibition. Overdose with single agents causing SRI or reversible inhibition of MAO (RIMAs) rarely cause serotonin toxicity; however overdoses of MAOIs alone can result in serotonin toxicity. Although the serotonergic toxicity of SSRIs increases with dose, SSRIs alone generally do not precipitate life threatening toxicity. Life threatening toxicity has occurred when MAOIs are combined with other serotonergic medicines.[1]

Whilst the pharmacology of serotonin toxicity is relatively simple, it is important to remember that it is not only prescription antidepressant medicines that can cause this toxicity. Non-prescription medicines, some illicit drugs and some complementary medicines can also affect serotonin concentrations. Therefore prescribers are advised to check with patients about use of over-the-counter or complementary medicines before prescribing serotonergic medicines.

A summary of serotonergic medicines is given in Table 1 below. Please be aware that this will change with time and is not exhaustive.

Table 1: Serotonergic substances

Serotonin Reuptake Inhibitors		
SSRIs	fluoxetine paroxetine sertraline	fluvoxamine citalopram escitalopram
Tricyclic antidepressants[a]	clomipramine	imipramine
SNRIs	venlafaxine sibutramine[b]	duloxetine
Opioid Analgesics	pethidine tramadol dextropropoxyphene	fentanyl methadone dextromethorphan[c]
Herbal (complementary)	St John's wort	
Monoamine Oxidase Inhibitors[d]		
Irreversible	phenelzine	tranylcypromine
Reversible	selegilene	moclobemide
Antibiotics	linezolid	isoniazid
Others	methylene blue (methylthioninium chloride)	
Serotonin Releasing Agents		
	Fenfluramine[e]	Amphetamines[f]
	MDMA (ecstacy)	
Others		
Antihistamines[g]	chlorphenamine	bromphenamine
Miscellaneous[h]	lithium	tryptophan

a Only these tricyclic antidepressants have serotonergic activity.

b Sibutramine although indicated for weight loss was an SNRI. Although this medicine has been withdrawn it has been found in 'herbal' weight loss products.

c Dextromethorphan is used as an anti-tussive and is available in supermarkets.

d Only MAOIs approved for use in New Zealand are listed here.

e Fenfluramine is not approved for use in New Zealand but has been found in 'herbal' weight loss products.

f Methylphenidate is not serotonergic, but methamphetamine ("P") may be.

g Not all commentators include these antihistamines as serotonergic.

h The evidence that triptans are serotonergic is controversial. The FDA has previously issued an alert but the pharmacology is not suggestive of an ability to provoke serotonin toxicity.

References

1. Gillman PK 2006 'A review of serotonin toxicity data: implications for the mechanisms of antidepressant drug action'. *Biol Psychiatry* 59: 1046-1051.
2. Sternbach H 1991 'The serotonin syndrome' *Am. J. Psychiatry* 148: 705-713.
3. Isbister GK, Buckley NA and Whyte IM 2007 'Serotonin toxicity: a practical approach to diagnosis and treatment' *Med J Aus* 187: 361-365.
4. Dunkley EJC, Isbister GK, Sibbritt D et al 2003 'The Hunter serotonin toxicity criteria: simple and accurate diagnostic decision rules for serotonin toxicity'. *Q J Med* 96: 635-642.

Iodine tablets for healthy pregnant and breastfeeding women

The Ministry of Health has recently issued advice to healthy pregnant and breastfeeding women to supplement their dietary intake of iodine.

The Ministry recommends that healthy pregnant and breastfeeding women take a daily 150 mcg iodine-only tablet from confirmation of pregnancy until the discontinuation of breastfeeding. This tablet should be taken in addition to eating well and choosing iodine-containing foods such as low-fat milk products, eggs, seafood, and commercially prepared bread.[1,2]

A brand of iodine tablets that is currently available in New Zealand is NeuroKare, made by Alaron in Nelson. Supplementation with an iodine tablet such as NeuroKare is recommended because it is difficult for pregnant or breastfeeding women to meet their increased requirements for iodine. Iodine is essential for the development of the brain and nervous system before birth, in babies, and in young children.

The Ministry's recommendations do not apply to women with pre-existing thyroid disease who should be individually managed to ensure normal thyroid function during pregnancy. Women who report high iodine intakes should have their iodine status assessed before further supplementing with an iodine tablet.

More information about the Ministry of Health's iodine recommendation is available at: **http://www.moh.govt.nz/moh.nsf/indexmh/nutrition-iodine**

A free health education leaflet, *Folic Acid and Iodine*, can be ordered for patients at: **http://www.healthed.govt.nz/resources/search-resources.aspx?q=iodine**

Acknowledgement: *Thank you to Barbara Hegan, Ministry of Health for contributing to this article*

References

1. Ministry of Health. 2006. Food and Nutrition Guidelines for Healthy Pregnant and Breastfeeding Women: A background paper.
2. See latest advice on food safety on the New Zealand Food Safety Authority's website at **http://www.nzfsa.govt.nz/**

Reducing the risk of GI reactions with NSAIDs and/or COX-2 inhibitors

Non-selective non-steroidal anti-inflammatory drugs (NSAIDs) have varying degrees of anti-inflammatory, analgesic and antipyretic effects. These effects are related to the inhibition of the cyclo-oxygenase isoenzymes COX-1 or COX-2 that are involved in the production of prostaglandins and thromboxanes.[1]

Gastrointestinal (GI) side effects occur commonly with all NSAIDs, including selective COX-2 inhibitors. These events are generally considered to be mediated by inhibition of COX-1, responsible for synthesis of the prostaglandins that inhibit acid secretion.[1] COX-2 selectivity should theoretically reduce the risk of GI adverse events; however studies have shown that COX-2 inhibitors still have a low affinity for COX-1.[2]

An analysis of reports sent to the Centre for Adverse Reactions (CARM) shows most patients experiencing GI adverse reactions with NSAIDs or COX-2 inhibitors had other risk factors for these events. Risk factors include: age greater than 65 years, history of peptic ulcer or gastrointestinal bleeding, previous gastric irritation with NSAID use, use of multiple NSAIDs or COX-2 inhibitors, and concomitant use of corticosteroids, anticoagulants and SSRIs.

For all patients requiring treatment with either a non-selective NSAID or COX-2 inhibitor, the extent and severity of gastrointestinal events can be reduced by:

- Using the lowest effective dose for the shortest duration possible.
- Avoiding the concomitant use of more than one NSAID, or a NSAID with a COX-2 inhibitor.
- Avoiding the concomitant use of aspirin and/or an anticoagulant where possible. If such a combination is necessary, a gastro-protective agent such as a proton pump inhibitor should be considered.
- Informing patients of, and monitoring for, signs and symptoms of gastrointestinal adverse events.

- Identifying patients with risk factors for serious GI adverse events and considering the use of a gastro-protective agent such as a proton pump inhibitor.

Healthcare professionals are encouraged to keep up-to-date with current prescribing information in product data sheets and applicable guidelines.

References:

1. Rang H., Dale M. and Ritter J. 1999. Pharmacology (4th Ed.) Edinburgh: Churchill Livingstone.
2. Pfizer New Zealand Ltd. 5 June 2009. Celebrex (celecoxib) data sheet. **http://www.medsafe.govt.nz/profs/Datasheet/c/Celebrexcap.pdf**

Global operation against illegal and counterfeit medicines

New Zealand recently took part in an international enforcement operation with over 40 countries throughout the world. The operation targeted the online sale of counterfeit and illegal medicines, and was designed to raise awareness of the dangers of buying medicines over the internet.

Operation Pangea III, carried out between 5 and 12 October of this year, resulted in multiple arrests across the globe and the seizure of over one million illicit and counterfeit pills.

In New Zealand the drug regulator Medsafe worked with the NZ Customs Service to intensively screen all mail entering the country during the week of the operation.

From over 400 consignments referred to Medsafe by the NZ Customs Service, 180 were detained because they were found to contain prescription medicines used for the treatment of conditions such as heart disease, diabetes, hair loss and erectile dysfunction. Oral contraceptives and antibiotics were also commonly found. Medsafe noted that these consignments were imported from 35 countries around the world.

Operation Pangea III indicates that consumers in New Zealand continue to self diagnose and self medicate for conditions requiring treatment that should only occur after consultation with a health care professional.

Health care professionals are advised to warn patients about the dangers of obtaining medicines over the internet and to consider this possibility if patients present with unexplained symptoms or possible adverse effects.

Medication error – confusion over Humalog insulins

Medication errors involving Humalog insulin products continue to occur in New Zealand hospitals.

Three Humalog products are currently available and funded in New Zealand: Humalog, Humalog Mix 25, and Humalog Mix 50. Errors continue to occur during the prescribing, dispensing and administration of these products.

There is potential for harm if a patient receives the wrong Humalog product, for example, the rapid acting Humalog when a combination rapid/intermediate acting Humalog Mix product is intended.

The following actions are recommended to prevent these errors occurring:

- Prescribe insulin using the full brand name and specify units in full.
- Highlight this potential for error to other healthcare professionals.
- Highlight the potential for error to patients prescribed Humalog or Humalog Mix.
- When using electronic prescribing or dispensing systems double check that the correct item from the drop-down menu has been chosen.
- Confirm with the patient (or carer) that the correct insulin is being prescribed, dispensed or administered.

The manufacturer of Humalog products has made changes to the product labels to help better distinguish between the different products. These changes followed similar issues experienced in Europe.

Quinine is not indicated for nocturnal leg cramps

Prescribers are reminded that quinine is no longer indicated for the treatment of leg cramps in New Zealand.[1]

CARM continues to receive reports of adverse events associated with the use of quinine for leg cramps, indicating that a significant number of patients are still being prescribed quinine for this off-label indication.

The safety of quinine was reviewed by the MARC in 2006 following local and international reports of thrombocytopenia after using this medicine for nocturnal leg cramps. An absence of data to support efficacy and clear evidence of harm led the MARC to conclude that the benefit-risk profile of quinine no longer supported an indication for the treatment of leg cramps.

The indication for prevention and treatment of nocturnal leg cramps was subsequently removed from quinine containing products in 2007. Quinine is now only indicated for the treatment of malaria and myotonia.

Similar changes to the indications for quinine have been made in Australia, the United Kingdom and the United States.

References

1. Medsafe. 2007. Quinine – not for leg cramps anymore. *Prescriber Update.* 28(1): 2-6.

Hypnotics and anxiolytics – a wake-up call

A recently released coroner's report serves as a reminder to all healthcare professionals that the use of benzodiazepines and other hypnotics needs careful consideration when used for the treatment of insomnia.

Importantly, the duration of use and dose of hypnotics and benzodiazepines should be limited to a short course of treatment with regular review.

Insomnia is distressing for the patient and can be challenging for healthcare professionals to treat. Before considering pharmacological treatment for insomnia other possible causes should be excluded.

If pharmacological treatment is initiated, a short-acting benzodiazepine or other hypnotic such as zopiclone can be used in the short-term. Patients should be given the lowest effective dose for the shortest possible time; regular review should include careful consideration of the need for ongoing treatment. Patients should also be informed about some of the less well known effects such as sleep walking and other dissociative behaviour e.g. sleep eating.

Patients who are treated long-term with benzodiazepines and other hypnotics for insomnia should be encouraged to gradually withdraw treatment. Slowly tapering the dose over a number of months may help to reduce the withdrawal effects such as agitation, anxiety and insomnia.

Further information on the treatment of insomnia, guidance on the safe prescribing of pharmacological treatment, and advice on withdrawing patients from long-term treatment is provided in the list of references below.[1-5]

Further information on the use of benzodiazepines and other hypnotics for the treatment of insomnia can also be found in the product data sheets at: **www.medsafe.govt.nz/profs/Datasheet/dsform.asp**

References

1. Tiller JWG (2003) The management of insomnia: an update. *Australian Prescriber.* Available at: **http://www.australianprescriber.com/magazine/26/4/78/81/** Accessed 24 November 2010.
2. Schutte-Rodin S, Broch L, Buysse D et al. 2010 Clinical guideline for the evaluation and management of chronic insomnia in adults. *Journal of Clinical Sleep Medicine* 4(5) 487-504.
3. BPAC (2008) Managing insomnia. Best Practice Journal. Issue 14. **http://www.bpac.org.nz/magazine/2008/june/insomnia.asp** Accessed 24 November 2010.
4. RANZCP (2008) Guidelines for use of benzodiazepines in psychiatric practice. Practice Guideline #5. Available at: **http://www.ranzcp.org/images/stories/ranzcp-attachments/Resources/College_Statements/Practice_Guidelines/pg5.pdf** Accessed 24 November 2010.
5. Therapeutic Guidelines Inc. Therapeutic Guidelines: Psychotropic Version 5 2003, Melbourne, Australia.

TEST YOUR KNOWLEDGE – end of year Prescriber Update quiz

Have you read *Prescriber Update* this year?
Have you kept up to date with emerging safety signals?
Test your knowledge with the end of year *Prescriber Update* quiz.

Answers to the quiz are available at:
www.medsafe.govt.nz/profs/PUarticles.asp

1. Why was dextropropoxyphene withdrawn in New Zealand?

2. Name five medicines used in New Zealand that are commonly associated with photosensitivity reactions.

3. What precautions need to be considered when switching brands of fentanyl patches?

4. On 1 December 2010, ketamine was reclassified to a:
   a) Prescription Medicine
   b) Class C(4) Controlled drug
   c) Class A Controlled Drug
   d) General Sales Medicine

5. Tramadol has been associated with cases of serotonin syndrome.
   True or False.

6. Name the medicine that has been associated with cases of male breast cancer this year.

7. How should the interaction between sodium valproate and the carbapenems be managed?

8. What is the difference between acitretin and isotretinoin?

9. Name three non-cardiac medicines that are associated with QT prolongation.

10. Omeprazole datasheets are being updated to include information about what type of electrolyte disturbance?

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