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AUSTRALIAN ADVERSE DRUG REACTIONS BULLETIN

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- ☆ New “Blue card” reporting form for ADRs
- ☆ High-dose vitamin B6 may cause peripheral neuropathy
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Please report **all** suspected reactions to these **Drugs of Current Interest**

Atomoxetine (Strattera)
Duloxetine (Cymbalta)
Ezetimibe and simvastatin (Vytorin)
Moxonidine (Physiotens)
Paliperidone (Invega)
Pramipexole (Sifrol)
Pregabalin (Lyrica)
Ranibizumab (Lucentis)
Rosuvastatin (Crestor or Viacor)
Sitagliptin (Januvia)
Strontium ranelate (Protos)
Varenicline (Champix)

1. New “Blue card” reporting form for adverse drug reactions

Prescribers are reminded that spontaneous reports of adverse drug reactions (ADRs) are critical to the early detection of safety signals once a medicine is marketed, and that the reporting of seemingly insignificant or common adverse reactions may help highlight previously unrecognised or important concerns. Thanks to you, Australia has one of the highest ADR reporting rates in the world and is a major contributor to the World Health Organisation, which collects ADR reports worldwide.

From August 2008 we are introducing a new version of the “Blue card” reporting form for ADRs. A copy of the form is included with this edition of the Bulletin.

We have consulted widely about what reporters would like and we hope the new form is easier to fill in. The major change is that the form is bigger! We are happy to receive further suggestions for the form; any good ideas will be considered for incorporation in later versions.

Note that you don’t have to use the new form although we encourage you to use it; we will continue to accept reports in any format as long as they include enough information and are legible. In addition to the form it is possible to report *via* the web, fax, email or phone; see the back page of the Bulletin for details.

If possible, all reports should contain the following information:

Patient information:

- Initials/UR No, DOB/age, gender

Medicine information, including:

- Medicine/s suspected of causing the reaction
- Any other medicines taken at the time
- Dates of starting and stopping the suspected and “other” medicine/s

Reaction information, including:

- A description of the reaction
- Date of onset of reaction
- Details of any treatment of the reaction
- Outcome of the reaction and outcome date

Reporter information:

- Name, address, phone, e-mail

The following (if available) would be very useful:

- Medical history
- Relevant laboratory data (haematology, biochemistry, imaging, serology, biopsy, etc)
- AUST L number for complementary medicines (located on the front of the product packaging)
- Batch number for vaccines and for all cases of suspected quality control (manufacturing fault) problems
- In cases where the outcome is fatal, the circumstances, date and cause of death. If a postmortem examination or coroner's enquiry was conducted, a copy of the report would also be useful.

Note: If any of the above information is contained in existing documentation (discharge summary, specialist report, laboratory data, etc), it can be provided as copies attached to the basic report.

We appreciate your continuing contributions.

2. High-dose vitamin B6 may cause peripheral neuropathy

The association between vitamin B6 (pyridoxine, pyridoxal, pyridoxamine) and neurotoxicity, particularly peripheral neuropathy, is well established and appears to be dependent on dose and duration of use.[1] However there may be a lack of recognition of the association amongst those who take or advocate the use of vitamin B6.

ADRAC has received two reports describing peripheral neuropathy with vitamin B6 products. In the first case, a 39 year old female taking 50 mg/day vitamin B6 for 3 months developed a feeling of burning pain and “electric shock” in her feet and lower legs. She was also taking a multivitamin product containing vitamin B6 and therefore her total daily dose most likely exceeded the upper level of intake of 50 mg/day recommended by the NHMRC.[2] Her symptoms resolved within 1 week of stopping the vitamins.

In the second case, a 69 year old female taking up to 600 mg/day vitamin B6 for 3-4 years developed persistent giddiness, wide-based gait and showed no response to vestibular retraining. Mixed

proximal sensory neuropathy was diagnosed and attributed to vitamin B toxicity. The patient had not recovered at the time of reporting and the outcome of this case is unknown.

ADRAC is concerned that the overuse of single vitamin products, use of multiple single-vitamin products (eg, oral and injectable forms of vitamin B6) or concomitant use of multivitamin products could result in some patients routinely exceeding the upper limit for vitamins associated with severe toxicity, such as vitamins B6 and A.

Patients presenting with unexplained neurological symptoms suggestive of peripheral neuropathy, such as tingling, burning and numbness of limbs, should be questioned about their vitamin B6 intake. All patients should be advised of the risks associated with excessive doses of vitamins.

Recently, the Complementary Medicines Evaluation Committee recommended to the TGA that the current warning statements required on the label for products containing 50 mg or more vitamin B6 per recommended daily dose be amended to provide more specific advice on the symptoms of vitamin B6 toxicity, and to include a warning to consumers to stop taking the product if tingling, burning or numbness is experienced and see a healthcare practitioner as soon as possible.[3]

References:
1. Renwick AG. Toxicology of micronutrients: Adverse effects and uncertainty. *J. Nutr* 2006; 136: 493S–501S.
2. http://www.nrv.gov.au/Nutrients.aspx?code=259662009
3: http://www.tga.gov.au/docs/html/cmec/cmecdr66.htm#i4

3. Desmopressin and hyponatraemia

Desmopressin (Minirin, Octostim) is a synthetic analogue of the natural antidiuretic hormone (ADH) arginine vasopressin and is currently available in nasal spray, nasal solution, tablet, sublingual wafer, and injection form. Desmopressin nasal spray and tablets are indicated for primary nocturnal enuresis (where an enuresis alarm has failed or is contraindicated) and cranial diabetes insipidus; desmopressin nasal solution and tablets are indicated for cranial diabetes insipidus and certain blood disorders.

Desmopressin acts on the ADH receptors in the kidneys, mimicking the effects of ADH and therefore preventing excessive loss of water. In the presence of excessive fluid intake in patients taking desmopressin, dilutional hyponatremia can occur. If this occurs quickly then lack of adaptation can result in a shift of water intracellularly and cerebral oedema, which may present with anorexia, nausea and vomiting, difficulty concentrating, confusion, lethargy, agitation, headache, and seizures.

The risk of hyponatremia is greater with desmopressin intranasal preparations than with the oral forms. In 2007, the TGA amended the indications for desmopressin nasal spray to restrict use only when it is not feasible to use an oral formulation. Sponsors were also required to amend all desmopressin product information documents to strengthen precautionary statements relating to the potential for hyponatraemia and to provide information on this potentially serious reaction.[1]

To date, ADRAC has received 68 reports of adverse reactions associated with the use of desmopressin, including 17 reports of convulsions (with or without reported hyponatremia), and 10 further reports of hyponatremia alone. Of 12 reports of convulsions or hyponatremia following the use of desmopressin nasal spray, 7 involved children under 13 years of age.

Prescribers are reminded that desmopressin nasal spray and tablets should be used in the treatment of nocturnal enuresis only when an enuresis alarm has failed or is contraindicated, and that tablets should be used in preference to intranasal preparations because of a possible increased risk of hyponatremia. Avoidance of excessive fluid intake should be advised during treatment with desmopressin. The ongoing need for these products should be reviewed periodically in patients taking desmopressin long-term.

Reference:
1. Ferring Pharmaceuticals Pty Ltd. Product Information for: Minirin Nasal Spray, Minirin Tablets, Minirin, Octistim.

WHAT TO REPORT? (you do not need to be certain, just suspicious!)

ADRAC encourages the reporting of all **suspected** adverse reactions to medicines, including vaccines, OTC medicines, herbal, traditional or alternative remedies. ADRAC particularly requests reports of:

*ALL suspected reactions to **new drugs** (see **drugs of current interest,** front page**)**
*ALL suspected drug interactions
*Suspected reactions causing
- •Death
- •Admission to hospital or prolongation of hospitalisation
- •Increased investigations or treatment
- •Birth defects

For blue cards
Reports of suspected adverse drug reactions are best made by using a prepaid reporting form ("blue card") which is available from the website: <http://www.tga.gov.au/adr/bluecard.pdf> or from the Adverse Drug Reactions Unit ☎ 02-6232-8744.

Reports can also be submitted electronically, by going to the TGA website <http://www.tga.gov.au> and clicking on “report problems” on the left, by fax: 02-6232-8392, or email: ADR.Reports@tga.gov.au

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The Bulletin is also available on the Internet at: **<http://www.tga.gov.au/adr/aadrb.htm>**

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