

RGH Pharmacy E-Bulletin

Volume 33 (6): March 16, 2009

A joint initiative of the Patient Services Section and the Drug and Therapeutics Information Service of the Pharmacy Department, Repatriation General Hospital, Daw Park, South Australia. The RGH Pharmacy E-Bulletin is distributed in electronic format on a weekly basis, and aims to present concise, factual information on issues of current interest in therapeutics, drug safety and cost-effective use of medications.

Editor: Assoc. Prof. Chris Alderman, University of South Australia – Director of Pharmacy, RGH

© Pharmacy Department, Repatriation General Hospital, Daw Park, South Australia 5041

Desvenlafaxine for depression

Desvenlafaxine (O-desmethylvenlafaxine) is the latest antidepressant to be subsidised under the auspices of the Pharmaceutical Benefits Scheme for the management of major depressive disorders. Desvenlafaxine, the major active metabolite of venlafaxine, is a serotonin and noradrenaline reuptake inhibitor (SNRI), with its clinical efficacy as an antidepressant theoretically due to the potentiation of these neurotransmitters in the central nervous system. It is marketed in Australia as Pristiq[®] and is available as desvenlafaxine succinate extended release tablets containing 50 mg or 100 mg of desvenlafaxine.

Desvenlafaxine has linear pharmacokinetics, an absolute bioavailability of 80.5%, and a mean terminal half-life of approximately 11 hours. About 45% of desvenlafaxine is renally excreted unchanged in urine; its metabolism is via conjugation and to a minor extent through CYP3A4. Desvenlafaxine has a noradrenaline binding affinity almost three times that of venlafaxine however the clinical significance of this is as yet unclear.

The usual recommended dose of desvenlafaxine is 50 mg once daily. While higher doses (from 100 mg to 400 mg daily) have also been studied, these have been associated with more frequent adverse effects and there is no clear evidence that they provide any additional benefit. In patients with renal impairment (creatinine clearance less than 30 ml/minute) it is recommended that the dose should be reduced.

Adverse effects of desvenlafaxine are similar to those seen with venlafaxine, and include nausea, dizziness, insomnia, and somnolence. Other potential adverse effects include dyslipidaemia, increased blood pressure, increased heart rate, hyponatraemia and mydriasis. On discontinuing, a gradual dose reduction is generally recommended as discontinuation symptoms may occur. Use of desvenlafaxine is contraindicated in those with a hypersensitivity to venlafaxine.

As with other medications that affect serotonin reuptake, use with other serotonergic drugs or those that impair metabolism of serotonin may lead to serotonin toxicity, a potentially serious condition. In terms of other drug interactions, potent inhibitors of CYP3A4 could potentially increase concentrations of desvenlafaxine. Desvenlafaxine has also been noted to have the potential to inhibit CYP2D6 and induce CYP3A4, potentially altering concentrations of other drugs metabolised by these enzyme systems.

The efficacy of desvenlafaxine in the treatment of depression has been demonstrated in randomised placebo-controlled trials. While providing yet another treatment option for major depressive disorders, there is no evidence that desvenlafaxine offers any advantage over its parent drug, venlafaxine, or any other antidepressants. It has been listed on the PBS on a cost minimisation basis compared with venlafaxine, however when venlafaxine becomes available as a generic formulation, the cost difference may well be reversed.

Acknowledgment – This E-Bulletin is based on work by Anita Marwood, Senior Clinical Pharmacist, RGH

FOR FURTHER INFORMATION – CONTACT THE PHARMACY DEPARTMENT ON 82751763 or email: chris.alderman@rgh.sa.gov.au
Information in this E-Bulletin is derived from critical analysis of available evidence – individual clinical circumstances should be considered when making treatment decisions. You are welcome to forward this E-bulletin by email to others you might feel would be interested, or to print the E-Bulletin for wider distribution. Reproduction of this material is permissible for purposes of individual study or research.