

RGH Pharmacy E-Bulletin

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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.

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Duloxetine

Yet another antidepressant has been launched in Australia and elsewhere, adding to the considerable array of choices available to clinicians seeking to use pharmacotherapy for the management of depression. Duloxetine, marketed in Australia as Cymbalta[®] and available as capsules containing 30 mg or 60 mg of the active ingredient.

Approved in Australia for the treatment of major depressive disorder, duloxetine is also used elsewhere for a range of other conditions including generalized anxiety disorder, management of neuropathic pain and for stress urinary incontinence. Duloxetine inhibits the neuronal reuptake of both serotonin and noradrenaline, although like other antidepressants the precise mechanism of action remains as yet unclear.

Duloxetine undergoes extensive hepatic metabolism, and the cytochrome P450 isoenzymes CYP2D6 and CYP1A2 are known to be involved in the metabolic clearance of the drug. The elimination half-life of duloxetine is approximately 12 hours. The use of a modified dosage is suggested for patients with severe impairment of renal function, and the drug should be avoided for those patients with severe hepatic impairment.

Clinically important adverse effects of duloxetine include nausea, dry mouth, constipation, insomnia, increased sweating, and changes in sexual function including decreased libido, delayed ejaculation, and erectile dysfunction. In addition, duloxetine can be associated with increased blood pressure and postural hypotension, decreased serum sodium (possibly because of syndrome of inappropriate antidiuretic hormone secretion), activation of mania/hypomania, and a discontinuation syndrome that can be observed after sudden withdrawal of treatment.

Duloxetine is a moderate inhibitor of cytochrome P450 2D6 and therefore may potentiate the effects of drugs that rely on this isoenzyme for a role in their metabolic clearance. On this basis, the combined use of duloxetine with drugs such as haloperidol, risperidone, perhexiline, metoprolol, flecainide and other CYP 2D6 substrates should be undertaken with considerable caution, or alternative therapy should be considered. As with other drugs that inhibit serotonin reuptake, the combined use of duloxetine with other agents that influence serotonin reuptake may create potential for the serotonin syndrome, a potentially serious drug interaction.

The safety of duloxetine during human pregnancy has not been established. Duloxetine is excreted into the milk of lactating women.

The usual approach to dosing involves administration at 60 mg once daily, although for those who have never been treated with the drug before (or where initial tolerability may be a concern) a lower starting dose of 30 mg once daily is used for one week before increasing the dose to 60 mg once daily. When discontinuing duloxetine after more than one week of therapy it is recommended that the dose be tapered to minimise the risk of discontinuation symptoms.

In Australia, supply of duloxetine for the management of major depression (but not other indications) is subsidised under the auspices of the Pharmaceutical Benefits Scheme.

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FOR FURTHER INFORMATION – CONTACT THE PHARMACY DEPARTMENT ON 82751763 or email: chris.alderman@rgh.sa.gov.au
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