

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.

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

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Ziprasidone

The 'atypical' or 'second generation' antipsychotics encompass a range of agents with a variety of chemical structures, receptor affinities and adverse effects. Their advantages over the older 'typical' agents include improved effectiveness against negative symptoms of schizophrenia and decreased incidence of extrapyramidal adverse effects. Ziprasidone is the latest agent in this group to be listed on the Pharmaceutical Benefits Scheme (Authority required) for the treatment of schizophrenia.

The efficacy of ziprasidone in schizophrenia is thought to be mediated through a combination of its antagonism of dopamine type 2 (D₂) and serotonin type 2 (5HT₂) receptors. It also exhibits antagonism of other receptors including histamine H₁ receptors and adrenergic α₁ receptors. It is indicated for the treatment of schizophrenia, related psychoses, prevention of relapse and for maintenance of clinical improvement during continuation therapy.

The recommended dose in the treatment of schizophrenia is 40mg twice daily taken with food. The dose may subsequently be increased up to 80mg twice daily, with dose adjustments occurring at intervals of not less than 2 days. Maintenance treatment should comprise the lowest effective dose (20mg twice daily may be sufficient). Ziprasidone is available as capsules of ziprasidone hydrochloride (Zeldox[®]) equivalent to 20mg, 40mg, 60mg and 80mg ziprasidone

Ziprasidone is extensively metabolised by aldehyde oxidase and by the hepatic enzyme CYP3A4 therefore dosage adjustment should be considered in the presence of mild to moderate hepatic impairment. The potential for interaction with inhibitors or inducers of CYP3A4 should also be noted.

Common adverse effects include somnolence, sedation, rash or urticaria, gastrointestinal disturbance, dizziness, headache, agitation, confusion, and orthostatic hypotension. Ziprasidone has been associated with prolongation of the QT interval (at a relatively low incidence) thus its use is contraindicated in recent acute myocardial infarction, uncompensated heart failure and conditions with a potential to increase QT interval. Concomitant use of drugs known to increase the QT interval is also contraindicated.

Randomised head-to-head clinical trials comparing ziprasidone and olanzapine suggest that the efficacy of ziprasidone may be lower than olanzapine, however this difference may be due to low initiation doses of ziprasidone as evidenced by high withdrawal rates due to lack of efficacy. To its advantage, ziprasidone has a favourable tolerability profile with a lower incidence of weight gain compared with olanzapine and other atypical antipsychotics, and possibly a lower potential for metabolic complications. As with other atypical antipsychotics, weight (BMI), waist circumference, blood pressure, fasting plasma glucose, and fasting lipid profile should be measured at commencement of therapy, and on a regular basis.

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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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