

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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Paliperidone

In late December 2006, the US Food and Drug Administration issued approval for the use of the new antipsychotic drug paliperidone, to be marketed under the brand name Invega®. The product will be presented as extended-release tablets to be used for the management of schizophrenia. The formulation uses osmotic pressure to deliver paliperidone at a controlled rate, and is made up of an osmotically active trilayer core surrounded by a subcoat and semipermeable membrane. The trilayer core is composed of two drug layers containing the drug and excipients, and a push layer containing osmotically active components. The water-dispersible coating erodes quickly in an aqueous environment such as the GI tract, and water then enters the tablet through the semipermeable membrane that controls the rate at which water enters the tablet core, ultimately determining the rate of drug delivery.

Paliperidone is actually the major active metabolite of another antipsychotic drug, risperidone. It shares fundamental pharmacological properties with the parent compound, including central dopaminergic D2 antagonism, antagonism at 5HT_{2a} receptors in the CNS, and antagonism at histaminic and adrenergic in the periphery.

Plasma concentrations of paliperidone gradually rise to a peak plasma concentration approximately 24 hours after oral administration. The recommended dose range for clinical use is 3 - 12 mg daily. The terminal half-life of paliperidone is approximately 23 hours, and thus steady-state concentrations are achieved after approximately 5 days. Preclinical trials suggest that extensive metabolisers and poor metabolisers of CYP2D6 do not differ significantly in their metabolism of paliperidone. No dose adjustment is suggested for patients with mild or moderate hepatic impairment, but the effect of severe hepatic impairment is yet to be determined. The dose should be reduced in patients with moderate or severe renal dysfunction.

Paliperidone should be used with caution for patients with diabetes mellitus, a history of seizure disorders, or with a history of falls or hypotensive episodes. The incidence of extrapyramidal side effects appears to be dose related, with the highest incidence observed at the upper end of the dose range.

The recommended dosage of paliperidone is 6 mg daily, although in some cases, 3 mg daily may be sufficient. Doses up to 12 mg daily may also be required in some cases. Dosage increments should not exceed 3 mg daily during the titration process. The tablets should be swallowed whole with ample fluid – do not crush, chew or divide the product.

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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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