

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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Solifenacin for overactive bladder

Overactive bladder is a condition characterized by symptoms of urge incontinence, urinary frequency and urgency, caused by involuntary contractions of the detrusor muscle in the bladder. Currently, the mainstay of treatment for this condition is the use of anticholinergic drugs. Recently a new medication, solifenacin (Vesicare[®]), has been approved for this indication in Australia.

Solifenacin

Solifenacin is a competitive muscarinic receptor antagonist and exerts its action by decreasing the contractions of the detrusor muscle. The contractility of this muscle is mediated by the M3 and M2 muscarinic receptor subtypes located in the bladder. Other muscarinic receptor subtypes are widespread in the body and have roles in cognition, saliva production and heart rate.

The potential advantage of solifenacin over other antimuscarinic drugs such as oxybutinin, tolterodine and atropine is that it has greater selectivity for M3 receptors. This suggests that solifenacin may be associated with a lower incidence of anticholinergic side effects. However, the most commonly reported side effects reported in clinical trials involving solifenacin were dry mouth, constipation and blurred vision, and comparative studies with other anticholinergics are currently lacking. In one long term study of solifenacin, dry mouth was reported by 21% of patients and was the most common reason for withdrawal from treatment.

Several large clinical trials have demonstrated that solifenacin is significantly more effective than placebo in improving urinary frequency, urgency, incontinence and nocturia. In a comparative study with tolterodine ER 4 mg, solifenacin the researchers reported that solifenacin was non-inferior to tolterodine for improving urinary frequency, but had greater efficacy than tolterodine for improving episodes of urgency and incontinence.

Solifenacin is metabolized in the liver by the CYP3A4 isoenzyme. Therefore, inducers or inhibitors of this enzyme may alter the pharmacokinetics of solifenacin. When administered simultaneously with CYP3A4 inducers (e.g. ketoconazole, cyclosporin, macrolide antibiotics) the maximum dose of solifenacin should be restricted to 5 mg. Although renal clearance of solifenacin is minor (7% of oral dose excreted unchanged), the drug should be used with caution in renal impairment, and doses greater than 5 mg are not recommended if creatinine clearance is <30 ml/min. Both severe renal impairment and moderate hepatic impairment result in approximately two-fold increases in the half-life of solifenacin.

Solifenacin is available in 5 mg and 10 mg tablets and the recommended starting dose is 5 mg once daily. The dose may be increased to 10 mg daily, but this has been associated with a significantly greater incidence of side effects. Currently, supply of solifenacin is not subsidised through the Pharmaceutical Benefits Scheme.

At this stage, due to the lack of comparative studies with other agents, solifenacin should not be considered as a first line agent for the management of overactive bladder, and should be reserved for situations where more commonly used anticholinergic drugs are not well-tolerated, or prove to be ineffective.

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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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