

# 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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## Sitagliptin

The serious morbidity and excess mortality associated with diabetes mellitus are well known, and given the high prevalence of diabetes in Australia and around the world, new treatment developments in this field are always greeted with considerable interest. Sitagliptin (Januvia) is a dipeptidyl peptidase 4 (DPP-4) inhibitor that is the first of a new class of oral antihyperglycaemic drugs to be marketed. Sitagliptin has recently been endorsed for subsidised supply under the auspices of the Australian Pharmaceutical Benefits Scheme (PBS) for dual oral therapy when used in combination with either metformin or a sulfonylurea, under circumstances where a patient cannot tolerate the combination of a sulfonylurea and metformin, but nevertheless requires dual therapy to achieve adequate glycaemic control.

Incretins are hormones that are released from the intestine after a meal, and help to control post-prandial and fasting blood glucose levels. There are two incretins of particular interest: glucose dependent insulinotropic polypeptide (GIP), and glucagon-like peptide -1 (GLP-1). These hormones potentiate glucose concentration-dependent insulin secretion. GLP-1 also inhibits glucagon secretion and delays gastric emptying. Incretins are rapidly metabolised by the DPP-4 enzyme. Sitagliptin is a DPP-4 inhibitor, and thus prolongs the action of incretins.

As yet studies have not elucidated mortality outcomes associated with the use of sitagliptin, but have used surrogate outcomes such as the effects of the drug upon HbA<sub>1c</sub> levels. Clinical trials have demonstrated that adding 100 mg of sitagliptin to metformin for a treatment period of 18-24 weeks resulted in reduced mean HbA<sub>1c</sub> (by 0.5-1.0% compared to placebo). Adding glipizide or rosiglitazone to metformin provided similar improvements to those achieved by adding sitagliptin to metformin therapy.

It must be emphasized, however, that the use of agents such as these should not delay the commencement of insulin, but may provide an alternative for patients who are reluctant to commence insulin. The other alternatives to sitagliptin are the glitazones, however these agents have recently been associated with adverse cardiac events and an increase in fracture risk, are therefore contraindicated for many patients. Sitagliptin is not indicated as monotherapy, or for use as triple therapy in combination with a sulfonylurea and metformin.

The usual dose of sitagliptin is 100 mg daily, which may be taken with or without food. Dosage reduction is required in moderate to severe renal impairment. For a creatinine clearance of 30-50 ml/min the recommended dose is 50 mg daily and for a creatinine clearance <30 ml/min a dosage of 25 mg daily is recommended.

Sitagliptin has not been associated with changes in weight or hypoglycaemia. Studies have shown that the common adverse effects were upper respiratory tract infections, nasopharyngitis, headache and nausea, and there have been post-marketing reports of severe hypersensitivity reactions. It is thought that sitagliptin may prolong the action of neuropeptides, including substance P, which may lead to a greater incidence of inflammatory and allergic reactions.

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**FOR FURTHER INFORMATION – CONTACT THE PHARMACY DEPARTMENT ON 82751763 or email: [chris.alderman@rgh.sa.gov.au](mailto:chris.alderman@rgh.sa.gov.au)**  
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