

# 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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## Fenofibrate

Fenofibrate is a fibric acid derivative. It improves lipid profiles by activating the peroxisome proliferator-activated receptor-alpha (PPAR $\alpha$ ) which results in increased lipolysis and clearance of atherogenic triglyceride (TG) rich lipoprotein. It predominantly has effects on TG, small dense LDL particles and HDL. Fenofibrate appears to be a full agonist of PPAR $\alpha$  where gemfibrozil is only a partial agonist.

In clinical studies, fenofibrate was shown to be better than statins at reducing triglycerides levels but not total cholesterol and LDL. A Combination of fenofibrate and another lipid lowering agent such as a statin or ezetimibe improved lipid levels to a greater extent than treatment with fenofibrate alone.

In terms of place of therapy for fenofibrate in the management of dyslipidaemia, it is clear that statins have established benefits in reducing cardiovascular morbidity and mortality, and this means that they are the first line option for reducing LDL cholesterol levels. Nonetheless, statins have less significant effects on TG and HDL which means that even with appropriate dose of statin therapy, some patients may still have residual cardiovascular risk (particularly in those with diabetes and metabolic syndrome). Patients with metabolic syndrome and type II diabetes commonly have atherogenic dyslipidaemia which consists of high TG, low HDL levels and the presence of small, dense LDL particles. Due to its lipid-lowering profile, fenofibrate may be preferred for use in atherogenic dyslipidaemia.

Additionally, combination therapy with a statin and fenofibrate may serve as a useful treatment option in patients with mixed dyslipidaemia. The FIELD trial, which was largely a primary prevention study, investigated the use of fenofibrate in patients with type II diabetes who did not have a compelling indication for lipid lowering therapy. Fenofibrate did not reduce CHD mortality or events, but more subjects in placebo arm received statins than those in fenofibrate arm.

According to the Australian National Prescribing Service (NPS) recommendations (2006), “a fibrate should be used first line, after lifestyle modification, in hypertriglyceridaemia. In mixed dyslipidaemia, a fibrate can be used first line when elevated triglyceride concentration is the predominant abnormality. Combination therapy may be required when both low-density lipoprotein-cholesterol (LDL-C) and triglyceride concentrations are moderately to markedly elevated.”

Retrospective analysis of adverse events from FDA databases showed that fenofibrate is associated with a lower incidence of rhabdomyolysis than gemfibrozil. Furthermore, the combination of fenofibrate and a statin was associated with fewer reports of rhabdomyolysis than the combination of gemfibrozil and a statin.

Fenofibrate has been available since 1975 but the original formulation had poor solubility. The new tablet formulation has improved bioavailability and can be taken without regard to food. It is available in Australia as 48 mg and 145 mg tablets. Dosage reduction is recommended in patients with renal impairment (creatinine clearance 20–60 mL/minute: 96 mg once daily, creatinine clearance 10–20 mL/minute: 48 mg once daily). Fenofibrate is subsidised for supply under the auspices of the Australian Pharmaceutical Benefits Scheme (PBS), although subsidised supply is restricted to specific circumstances that are stipulated in the PBS schedule.

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