

# 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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## Prasugrel

Prasugrel (Effient®) is the latest addition to the thienopyridine class of medications (e.g. clopidogrel, ticlopidine). This drug is an irreversible antagonist of P2Y<sub>12</sub> ADP receptor on platelets; thereby inhibiting platelet activation and aggregation. Currently, when co-administered with aspirin, prasugrel has an approved indication in Australia for prevention of atherothrombotic events in patients with acute coronary syndromes (ACS), defined as moderate to high risk unstable angina, ST-segment elevation myocardial infarct (STEMI) or non-STEMI, who are to undergo percutaneous coronary intervention (PCI).

Prasugrel is a prodrug and is rapidly metabolised to a pharmacologically active metabolite and inactive metabolites. It is primarily metabolised by CYP 3A4 and CYP 2B6 and to a lesser extent by CYP 2C9 and CYP 2C19 (10-20% contribution). Oral bioavailability is more than or equal to 79%. and its elimination half life of approximately 7.4 hours. Approximately 70% of the prasugrel dose is excreted in the urine and 25% in the faeces.

Prasugrel is available as 5mg and 10mg tablets. The manufacturer recommends a loading dose of 60 mg and followed by maintenance doses of 10mg once daily. No dose adjustment is required in patients with renal impairment or for those with mild to moderate hepatic impairment. Patients with severe hepatic disease should not be using prasugrel due to the potential risk of bleeding.

The current practice is to use aspirin plus clopidogrel in patients with ACS undergoing PCI unless contraindicated. A number of clinical trials have shown that prasugrel (at the currently studied doses) inhibits platelet activation and aggregation more rapidly and consistently than clopidogrel. In the TRITON-TIMI 38 study, prasugrel was compared with clopidogrel in 13608 patients with ACS who were undergoing PCI. The results of the study showed that primary endpoints (composite of death from cardiovascular causes, non-fatal myocardial infarction or non-fatal stroke) at 15 months after study initiation were significantly lower with prasugrel (9.9%) compared to clopidogrel (12.1%) (Absolute Rate Reduction of 2.2% with 95% CI)

The TRITON-TIMI 38 study did however show an increase risk of bleeding (including TIMI major & minor bleeding, CABG and non-CABG related TIMI major bleeding) in the prasugrel group compared to clopidogrel. Further analysis show that in three specific subgroups of patients (those over 75 years of age, those weighing less than 60kg and those who had a previous stroke or transient ischemic attack) actually had net harm from use of prasugrel.

At the time of publishing, there have been no clinically significant interactions associated with CYP450 isoenzymes reported with prasugrel. However, it is important to exercise caution when using it with other drugs that increase risk of bleeding. It is also important to note that the drug is a weak inhibitor of CYP2B6 and drugs with narrow therapeutic index (e.g. cyclophosphamide) metabolised by this isoenzyme might be affected.

Prasugrel has received registration approval from the Therapeutic Goods Administration (TGA), Australia as of June 2009 for the aforementioned indication. However, it is not currently subsidised for supply through the Pharmaceutical Benefits Scheme (PBS).

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