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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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Rivaroxaban

The current approach to prophylaxis for venous thromboembolism (VTE) after major orthopaedic surgery of the lower limbs includes the use of warfarin, unfractionated heparin or low molecular weight heparin (refer to e-bulletin vol 31(8)). These require regular monitoring for dosage adjustments, as well as parental administration (in the case of heparin/heparinoids): this can be inconvenient for patients and carers, especially in out-patient settings.

Rivaroxaban (Xarelto®) is a selective direct Factor Xa inhibitor with good oral bioavailability. Factor Xa converts prothrombin to thrombin via the prothrombinase complex. This eventually leads to formation of fibrin clot and platelet activation. Rivaroxaban has a rapid onset of action, a half-life of 5-9 hours and is predominantly renally eliminated.

The recommended dose of rivaroxaban is 10mg daily, which may be taken with or without food. Rivaroxaban can be initiated 6-10 hours after surgery in patients with established haemostasis. The manufacturer recommends treatment duration of five weeks for hip replacement surgery and two weeks for knee replacement surgery. Dose adjustment for patients with mild to moderate renal impairment is not necessary, however, rivaroxaban is regarded as contraindicated for those with severe renal impairment (CrCl <15 ml/min). The manufacturer also stipulates that the drug is contraindicated in patients with hepatic disease.

In the RECORD-1 study, patients with total hip replacement were randomised to receive 5-10 mg of rivaroxaban or 40 mg enoxaparin for 35 days: rivaroxaban had similar efficacy and safety to enoxaparin. This finding was also shown in the RECORD-2 study, where rivaroxaban was significantly more effective than enoxaparin in prevention of VTE in hip arthroplasty (ARR 7.5% with 95% CI). However, the duration of therapy varied, as the rivaroxaban treatment group received 31-39 days of therapy, whereas enoxaparin group received 10-14 days. In RECORD-3, rivaroxaban was statistically superior to enoxaparin in preventing VTE, with similar rates of bleeding, for patients undergoing total knee replacement (ARR 9.2%).

Rivaroxaban is associated with bleeding, anaemia, nausea and a temporary increase in some liver enzymes. In the RECORD-2 trial, there was a small increase in cardiovascular events in rivaroxaban group after stopping treatment (in comparison to the control group); further research is needed to assess the implications of this finding.

Ximelagatran (a thrombin inhibitor) was withdrawn from the market by the manufacturer in 2006 because of concerns about potential liver toxicity. Although there was no increase in hepatic toxicity in rivaroxaban group in RECORD trials, further safety data is required.

A trial comparing rivaroxaban with warfarin for the prevention of VTE and prevention of cardioembolic events in patient with atrial fibrillation is currently in progress.

Rivaroxaban has been recently approved in Australia for prevention of VTE in patients undergoing elective total hip or knee replacement.

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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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