

This bulletin aims to provide a snapshot of current evidence-based reports and journal articles relevant to general practice teams and pharmacists.

## Dabigatran (Pradaxa) for preventing venous thromboembolism after hip or knee replacement surgery

NPS RADAR; 10 April 2010

Dabigatran is a new oral anticoagulant (a direct thrombin inhibitor), which has been approved for short term use after hip or knee replacement surgery. The recommended duration of therapy is 10 days after knee replacement and 28–35 days after hip replacement.

It appears to have similar efficacy to that of enoxaparin 40 mg once daily after knee or hip replacement, however, a clinically important difference between the two drugs cannot be completely ruled out. While dabigatran also appears to have broadly similar efficacy to both rivaroxaban and fondaparinux, this has not been tested in head-to-head trials.

Bleeding rates with dabigatran are similar to those with enoxaparin. Dabigatran is also contraindicated in hepatic impairment that is expected to have an impact on survival and in severe renal impairment (creatinine clearance < 30 mL/min).

**Prescribers' Guide:** This is the first new oral anticoagulant since warfarin. It is approved, however, only for short-term use after hip or knee replacement surgery.

## Ten per cent cross-sensitivity between penicillins and cephalosporins questioned

Medicine Q and A's prepared by UKMi pharmacists for NHS; Jan 2010

*Drug & Therapeutics Bulletin* 1996; 34 (11): 87 – 88

*Annals of Allergy, Asthma & Immunology* 1995; 74: 167 – 170

*Canadian Journal of Hospital Pharmacy* 2005; 58 (2): 90 – 96

*The Journal of Family Practice* 2006; 55 (2): 106 – 112

*British Medical Journal* 2007; 335: 991

*Drug Safety* 1994; 10 (4): 318 – 327

*Otolaryngology-Head and Neck Surgery* 2007; 136: 340 – 347

*Pediatrics* 2001; 108 (3): 798 – 808 & 2004; 113: 1451 – 1466 & 2005; 115: 1048 – 1057



It is commonly taught that approximately 10 per cent of patients who are allergic to penicillin will have an adverse reaction to cephalosporins. However, this widely cited rate of cross-sensitivity has been questioned as it appears to be based on data from the 1960s and 1970s and results of invitro (immunological) tests that were not supported by clinical skin tests in penicillin-sensitive patients. A meta-analysis published in 2007 has identified the reasons why this cited cross-sensitivity may be an overestimate.

Recently the American Academy of Paediatrics (AAP) has recommended prescribing cephalosporins in patients allergic to penicillin for sinusitis or otitis media. A review of the evidence to support this recommendation concluded that coincidental allergic reactions to cephalosporins might occur amongst penicillin/amoxicillin allergic patients. There appears to be a predictable, immunological reason for cross-reactions with first generation cephalosporins. However, most second and third generation cephalosporins are unlikely to be associated with cross-reactivity due to differences in their chemical structures. In Australia, the Australian Medicines Handbook states that cephalosporins are contraindicated in patients with a history of allergy to penicillin. The Therapeutic Guidelines state that anaphylactic responses to penicillin occur approximately once for every 10,000 courses administered, with 10 per cent of these reactions being fatal, most often associated with parenteral rather than oral administration.

**Prescribers' Guide:** In Australia, there is no document similar to the AAP review, which now recommends specific cephalosporin antibiotics for treating penicillin allergic patients with sinusitis or otitis media. Prescribers should continue to seek specialist advice before using cephalosporin antibiotics in any patient with an immediate hypersensitivity reaction to penicillin antibiotics.

## Could long-term analgesic use increase risk of deafness?

Am J Med 2010; 123: 231-7

A large epidemiological study from the U.S. found a small increased risk of hearing loss associated with long term use of analgesics (aspirin, NSAID, and paracetamol). This is a study of observation and association and does not prove that these medicines caused the hearing loss. Analgesics are very valuable in treating a variety of disorders, so caution is needed in interpreting results that show an association but do not prove causality.



**Prescribers' Guide:** The increased risk for hearing loss with long-term analgesic use is small, and the results of this study should be interpreted with caution.

## FDA approves rosuvastatin for primary prevention of cardiovascular disease

FDA News Release Feb.9, 2010

<http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm199891.htm>

Based on the results of the placebo-controlled JUPITER trial, the U.S. Food and Drug Administration (FDA) has recently approved rosuvastatin (Crestor™) for the primary prevention of cardiovascular disease. This is to reduce the risk of stroke, heart attack, and the risk of arterial revascularisation procedures (including coronary artery bypass graft, or bypass grafting of a peripheral artery or carotid artery, or angioplasty or stent placement). Therefore people in the U.S. who have no clinically evident heart disease and with 'normal' low-density lipoprotein (LDL) cholesterol levels but are at an increased risk of heart disease due to the combined effect of the following risk factors can use rosuvastatin:



- age (> 50 years in men; > 60 years in women), and
- an elevated high-sensitivity C-reactive protein level (> 2 mg/L), and
- the presence of at least one additional cardiovascular risk factor (e.g. high blood pressure, low HDL-C, smoking, or a family history of premature heart disease).

**Prescribers' Guide:** In Australia, rosuvastatin is licensed as an adjunct to diet in treating hypercholesterolaemia, not yet for primary prevention of cardiovascular disease.

## New laxative listed on PBS for opioid induced constipation in palliative care

NPS RADAR; March 2010

Methylnaltrexone is a subcutaneous injection for use in palliative care patients with opioid-induced constipation that has not responded to adequately titrated laxatives, and in whom bowel obstruction has been excluded. It is not a treatment for constipation caused by factors other than opioids.

Methylnaltrexone relieves constipation by reversing the effect of opioids in the peripheral nervous system but does not reverse opioid analgesia as it is unable to cross the blood-brain barrier when given in clinically appropriate doses. Ensure that toileting facilities are accessible, as bowel movements may occur within 30 minutes of an injection.

**Prescribers' Guide:** Methylnaltrexone is listed on the palliative care schedule for the treatment of opioid-induced constipation that has failed to respond to laxatives, in combination with oral laxatives.

## Small Doses out of repeats

This is the final edition of Small Doses. We thank our many readers for their interest in this bulletin since its launch in May 2008. We particularly acknowledge editor, Janet McNeece, and **gpns** Pharmacist Adviser, Sue Edwards, for compiling Small Doses each month. We will now incorporate news and updates about the quality use of medicines in future editions of **gpns's** quarterly newsletter for general practice teams, *Success in Practice* and weekly bulletin, *Wednesday in the South*.

Please contact **gpns** Corporate Communications Adviser, Sheryl Klingner, on 8374 7000 with any suggestions for medicines-related topics to be covered in our publications.

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