Updated data sheet for dabigatran

Dabigatran is a new oral anticoagulant that has been available fully subsidised on the Pharmaceutical Schedule since 1 July 2011.

The dabigatran data sheet[1] was updated in early November 2011 to highlight the importance of an assessment of renal function in people who may be suitable for treatment with dabigatran, and also for those already on treatment. Moderate renal impairment in people taking dabigatran is associated with an increased risk of bleeding and in addition, dabigatran is contraindicated if the creatinine clearance is < 30 mL/min. There have been no changes to the recommended doses.

The key changes to the data sheet are:

- Renal function must be assessed in all patients prior to the initiation of dabigatran
- For patients taking dabigatran, renal function should be rechecked in any clinical situation where a decline in renal function is suspected, e.g. dehydration, hypovolaemia and with some medicines such as diuretics
- Renal function should be assessed at least annually in patients taking dabigatran aged over 75 years or with moderate renal impairment (creatinine clearance 30–50 mL/min)

Although eGFR provides an estimate of renal function it may not be accurate enough in older people or people with a BMI <18.5 kg/m^2 or > 30 kg/m^2. Therefore it is safer to calculate creatinine clearance for the majority of people. Creatinine clearance can be calculated with the Cockcroft-Gault equation or determined using a hand held or electronic (online or PMS) calculating tool.

The formula for calculating creatinine clearance is:

$$\text{Creatinine clearance (mL/min)} = \frac{(140 - \text{age}) \times \text{weight (kg)} \times \text{constant}^*}{\text{serum creatinine (µmol/L)}}.$$

* The constant = 1.23 for men, 1.04 for women

Dabigatran dosing regimen

Check creatinine clearance.

When a patient is changing from warfarin to dabigatran, discontinue warfarin and do not initiate dabigatran until the INR is <2.0.

The recommended dose of dabigatran for the prevention of stroke in people with non-valvular atrial fibrillation is:

- 150 mg, twice daily, if creatinine clearance >30 mL/min
- 110 mg, twice daily, if age ≥80 years

The updated data sheet also states that the lower 110 mg dose, twice daily, may be considered in patients aged 75 to 80 years if the patient's thromboembolic risk is low and their bleeding risk is high.

The recommended dose of dabigatran for the prophylaxis of VTE following major orthopaedic surgery is 110 mg, one tablet on the day of surgery then:

- 220 mg (110 mg x 2), once daily, if creatinine clearance >50 mL/min
- 150 mg (75 mg x 2), once daily, if creatinine clearance 30-50 mL/min

N.B. The length of the treatment course after surgery varies with the type of surgery. Prophylaxis post knee replacement is for ten days while for hip replacement it is 35 days.

The main adverse risk of dabigatran is bleeding. Although the manufacturer states that so far, reports of patients with serious or fatal bleeding are no different to expected rates, care must be taken when using dabigatran in patients at increased risk of bleeding. Risk factors for bleeding include:

- Age ≥75 years
- Moderate renal impairment (creatinine clearance 30–50 mL/min)
- Recent gastrointestinal bleeding
- Concomitant use of medicines such as aspirin, clopidogrel, NSAIDs, SSRIs

Any bleeding events in people taking dabigatran should be reported to the Centre for Adverse Reactions Monitoring (CARM). Reports can be made via bestpractice Decision Support ("Adverse drug reaction reporting" module), or directly with CARM; using a CARM reporting card, online at: **https://nzphvc-01.otago.ac.nz/carm**, phone: 03 479-7247, fax: 03 479-7150 or email: carmnz@otago.ac.nz

The approved indications for dabigatran use in New Zealand have been more specifically defined and are:

- The prevention of stroke in patients with non-valvular atrial fibrillation and at least one other risk factor for stroke (e.g. previous transient ischaemic attack or stroke, left ventricular ejection fraction < 40%, symptomatic heart failure, age ≥75 years, age ≥65 years plus diabetes or hypertension or coronary artery disease)
- For prophylaxis of venous thromboembolic events after major orthopaedic surgery

For further information see: "The use of dabigatran in general practice", BPJ 38 (Sep, 2011).

Reference:

1. Boehringer Ingelheim (NZ) Ltd. Dabigatran etexilate (Pradaxa). Medicine data sheet. Available from: www.medsafe.govt.nz (Accessed Nov, 2011).