quality safe use of medicines

Medication Alert

Urgent: acute haemorrhage associated with Dabigatran initiation causing hospital admissions

Alert 11 July 2011

For the attention of: General Practitioners, Community Pharmacists, Medicines Advisory Committees or Medication Safety Committees
For information to: Aged residential care providers

Purpose of this alert

- To highlight the risks associated with the use of dabigatran

Required Action

Prior to starting therapy with dabigatran in any patient check:

1. What is the indication? These are the only two licensed indications in New Zealand:
   - atrial fibrillation (prevention of stroke, embolism, and reduction of vascular mortality)
   - VTE prophylaxis post major orthopaedic surgery
2. Is the patient on warfarin? If yes, stop the warfarin and monitor INR.
   Do **NOT** start dabigatran until INR is less than 2. There is a high risk of bleeding if dabigatran started when INR> 2.
3. Does the patient have renal impairment?
   - Do not prescribe dabigatran to patients with creatinine clearance (CrCl) less than 30ml/min.
   - If CrCl is between 30-50ml/min prescribe a lower dose (as per data sheet for VTE prophylaxis).

   The data sheet recommends CrCl calculated using the Cockcroft and Gault equation. If using a laboratory reported e GFR please be aware of patients for whom this is not accurate. If in doubt calculate CrCl using Cockcroft and Gault

   $$\text{CrCl mL/min} = \frac{(140 - \text{age}) \times \text{lean body weight (kg)}}{\text{Plasma creatinine (micromol/L)} \times 0.815} \times 0.85 \text{ if female}$$

   Some practice management systems have a CrCl calculator but check that the units match the units reported by your laboratory. There are also CrCl calculators available on the net.
4. Does the patient have haemorrhagic risk factors? Avoid use in these patients because of the bleeding risk.
5. Are there known problems with the patient's adherence to medicine taking? There is a rapid loss of effect if doses of dabigatran are missed.
6. Are there any potential interactions? While not as prevalent as those associated with warfarin, there are serious interactions. In particular, concomitant clopidogrel and aspirin will increase the risk of bleeding and advice should be sought from a specialist before co-prescribing. Other serious interactions have been described. Please check using MIMS drug interaction alert.

Required Action

Once the decision to prescribe has been made, inform the patient:

1. **To report any suspicion of bleeding immediately—there is no antidote to dabigatran induced bleeding** and a complex combination of measures may be required to contain the bleeding.
2. Good compliance/adherence is vital because there is a rapid loss of effect if doses are missed.
3. Dabigatran can only be dispensed in original packs and can not be packed into a compliance pack or pill box i.e. do not transfer out of the original pack for any reason because of the stability of the product.
4. Crushing the tablets or opening the capsules is not recommended because of the stability of the product.
5. Consult with a health professional before taking aspirin or a NSAID.

Case studies of two reported hospital admissions

Mr X

- Mr X (92 year old rest home resident), diagnosed AF June 2011, started on warfarin for stroke prevention. Last known INR 4.0 on 1.7.11. Admitted to hospital on 7.7.2011 with melaena.
- 4.7.11 Mr X given his usual dose of warfarin (3mg) by rest home nursing staff.
- 5.7.11 Warfarin stopped, CrCl 33mL/min and he was commenced on dabigatran 150mg twice daily.
- 7.7.11 Mr X had melaena in the morning and was sent to hospital by ambulance. His INR was 12 and CrCl 23mL/min. At 13.35 he was given vitamin K 10mg, 2 units of fresh frozen plasma, prothrominex and tranexamic acid. Gastroscopy showed gastritis with probable bleeding from gastric erosions.
- 12.7.11 Mr X was discharged with the recommendation made that he should not be on either warfarin or dabigatran.

Mr B

- Mr B (82 year old), PMH; chronic AF, AVR, CCF and IHD. Admitted to hospital 11.7.11 with PR bleeding, increased shortness of breath and chest pain.
- 7.7.11 Warfarin stopped, dabigatran 110mg bd commenced.
- 11.7.11 Calculated CrCl 23mL/min, treated with Prothrominex, fresh frozen plasma, Vitamin K and red blood cells.

Main learnings from the cases:

- Stop warfarin and check INR is < 2 before starting on dabigatran.
- Check dose is correct for age: patients over 80 years of age require a lower dose.
- Check renal function before starting dabigatran.

Background to this Safe Use of Medicines Alert

- Since 1 July 2011 when dabigatran was fully funded for community prescribing, there have been reports of hospital admissions with bleeding (mainly gastrointestinal) related to dabigatran treatment.
- Patients should be monitored for signs of bleeding and anaemia at each appointment. If bleeding is suspected, discontinue dabigatran, check thrombin time and activated partial thromboplastin time and discuss with a haematologist or cardiologist.
- Dabigatran is a direct thrombin inhibitor with a predictable dose response and does not require regular blood testing during treatment.
- Clinical experience with dabigatran is limited.
- Interactions: the interactions identified are less than with warfarin but some interactions have been identified that could result in an increased bleeding risk. Please check for potential interactions when prescribing dabigatran.

For an electronic version of this alert download from the website, www.safeuseofmedicines.co.nz or contact Beth Loe, beth.loe@hqsc.govt.nz

If you require any further information or wish to provide feedback on this alert, please go to www.safeuseofmedicines.co.nz