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SAFER USE OF HIGH RISK MEDICINES

Waitemata District Health Board

Best Care for Everyone

DABIGATRAN - SAFE PRESCRIBING - NOT A MAGIC BULLET

- INFORM PATIENTS TO REPORT ANY BLEEDING IMMEDIATELY
- BLEEDING MAY REQUIRE URGENT REFERRAL
- CHECK RENAL FUNCTION BEFORE PRESCRIBING - USE THE CORRECT DOSE
- CONSIDER POTENTIAL INTERACTIONS AND ADVERSE EFFECTS
- COMMUNICATE GOOD COMPLIANCE AND APPROPRIATE ADMINISTRATION

Dabigatran etexilate is a direct thrombin inhibitor. It is indicated for the prevention of stroke, systemic embolism and reduction of vascular mortality in patients with non-valvular atrial fibrillation (AF). It is also indicated for the prophylaxis of venous thromboembolism (VTE) post major orthopaedic surgery, for the treatment of acute VTE, and for the prophylaxis of recurrent VTE. Dabigatran must not be given to patients with prosthetic heart valves.

INFORM PATIENTS TO REPORT ANY BLEEDING IMMEDIATELY

As with all anticoagulants, there is a risk of bleeding; inform patients to report any signs of bleeding immediately.

Avoid giving dabigatran to patients with haemorrhagic risk factors including gastrointestinal bleeding, recent trauma, haemorrhagic stroke (within 6 months) or following brain, spinal or ophthalmic surgery. The risk of bleeding may also be increased in:

- patients over 75 years old
- patients with moderate renal impairment (CrCl 30-50mL/min)
- concomitant treatment with antiplatelet agents
- previous gastrointestinal bleed

for these patients a dose reduction is usually recommended. See information box (over)

BLEEDING MAY REQUIRE URGENT REFERRAL

Monitor patients for signs of bleeding at each appointment and check for symptoms of anaemia. If there is any bleeding, discontinue dabigatran, check TT and aPTT, note when the last dose was taken, and discuss with a haematologist or cardiologist. A combination of intensive interventions may be required to contain the situation. A dabigatran reversal agent is available in a trial setting at Auckland, Middlemore and North Shore Hospitals for patients requiring urgent reversal or who require urgent surgery/procedures.

Fatal haemorrhage associated with dabigatran is more prevalent in older patients. Because routine monitoring of dabigatran is not required, please ensure the patient understands they must report any unexplained bruising or bleeding immediately.

CHECK RENAL FUNCTION BEFORE PRESCRIBING – USE THE CORRECT DOSE

Calculate creatinine clearance (CrCl) based on lean body weight (or actual body weight if the patient is lean) before prescribing, and every 6-12 months while on treatment. Dabigatran must not be given to patients with severe renal impairment (CrCl less than 30mL/min) and should be discontinued if acute renal failure develops during treatment.

Reassess CrCl if the patient becomes dehydrated, or if they take medicines that could further compromise renal function (eg diuretics or NSAIDs).

Patients who have moderate renal impairment (CrCl 30-50mL/min) may require a lower dose. See information box (over). Older patients and patients with unstable renal function are at risk of undertreating or overtreating with fixed doses of dabigatran; other anticoagulants may be more suitable.

Note: Dabigatran is best avoided in patients with severe liver disease, especially if the prothrombin time is prolonged.

CONSIDER POTENTIAL INTERACTIONS AND ADVERSE EFFECTS

Concomitant administration with **ketoconazole** is contraindicated due to the increased dabigatran plasma concentrations and the increased risk of bleeding.

Amiodarone, **verapamil**, **quinidine** and **clarithromycin** are also expected to result in increased dabigatran plasma concentrations. Combinations with **amiodarone** and **verapamil** are best avoided but if they must be given, either reduce the dose of dabigatran, or dose at different times of day and monitor closely for signs of bleeding.

Rifampicin reduces the exposure of dabigatran, so is best avoided.

St John's Wort, phenytoin and **carbamazepine** are also expected to reduce the efficacy of dabigatran, and should be avoided if at all possible.

Concomitant treatment with **clopidogrel**, **aspirin** or **dipyridamole** will increase the risk of bleeding, and caution is advised when using **NSAIDs**. Concurrent use of **SSRIs** or **SNRIs** may also increase the risk of bleeding.

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DABIGATRAN

COMMUNICATE APPROPRIATE ADMINISTRATION AND GOOD COMPLIANCE

To reduce the risk of oesophageal ulceration, advise all patients to swallow the capsules whole with a large glass of water, and preferably with food. If possible, patients should remain upright after swallowing the capsules. Dabigatran must not be crushed or chewed, and it is not suitable for patients who have oesophagitis or difficulty swallowing. Ask patients to report any symptoms of dyspepsia or 'heart burn' during treatment.

Good compliance with dabigatran is vital, there is a rapid loss of effect if doses are missed. Make sure the patient is aware of this, and consider other options if there are any concerns about compliance. Dabigatran must be kept in the original pack because there is a loss of stability once opened. Dabigatran is not suitable for re-packing into compliance aids like Webster® or Medico® packs.

Atrial fibrillation (AF)

Dabigatran may be a useful alternative for patients with AF who are not managing the monitoring requirements for warfarin, or are not well controlled. Patients who are currently prescribed aspirin because of concerns about interactions with warfarin or regular testing, may benefit from dabigatran instead of aspirin.

Compliance with twice daily dosing is very important. If there are uncertainties about dabigatran, obtain specialist advice. For patients who are well controlled with warfarin, there is little reason to change treatment.

Venous thromboembolism (VTE)

Dabigatran is indicated for the treatment and prevention of VTE under certain circumstances. Note that the dose and frequency varies depending on indication and renal function. For the treatment of VTE, dabigatran should be started after the patient has received at least 5 days of parenteral anticoagulant therapy. Dabigatran may then be given as a twice daily dose for up to 6 months.

ACKNOWLEDGEMENTS

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KEY REFERENCES

1. Boehringer Ingelheim (NZ) Limited. Dabigatran etexilate Pradaxa® New Zealand Datasheet July 2014 www.medsafe.govt.nz/profs/datasheet/p/Pradaxacap.pdf (Accessed 29-09-14)
2. New Zealand Formulary, dabigatran. http://nzf.org.nz/nzf_1502.html?searchterm=dabigatran (Accessed 14-10-14)

DOSING INFORMATION

ATRIAL FIBRILLATION (Prevention of stroke, systemic embolism and reduction of vascular mortality).

Age	Dose
18-74y	150mg twice daily
75-80y (if low thromboembolic risk and high bleeding risk)	110mg twice daily
80y and older	110mg twice daily
Renal impairment	
Moderate (CrCl 30-50mL/min)	110mg twice daily
Severe (CrCl <30mL/min)	do not prescribe
PREVENTION OF VTE following major orthopaedic surgery	
Knee replacement surgery:	
1-4 hours following surgery	110mg
Days 2-10 postoperatively	220mg once daily
Hip replacement surgery:	
1-4 hours following surgery	110mg
Days 2-28 or 2-35 postoperatively	220mg once daily
Renal impairment:	
Moderate (CrCl 30-50mL/min)	150mg once daily
Severe (CrCl <30mL/min)	do not prescribe
PREVENTION OF RECURRENT VTE	
Ongoing treatment depending on individual risk	150mg twice daily
Renal impairment	
Severe (CrCl <30mL/min)	do not prescribe
TREATMENT OF VTE	
Following parenteral anticoagulant for at least 5 days	150mg twice daily (up to 6months)
Renal impairment	
Severe (CrCl <30mL/min)	do not prescribe

Note: The majority of dosing data is for patients weighing 50-100kg. There is no dosing or safety information for patients under 18 years old, during pregnancy or lactation. Enoxaparin should be used for VTE in pregnancy; warfarin is the treatment of choice when breastfeeding.

CLICK HERE FOR MORE INFORMATION ON DABIGATRAN AND A FULL REFERENCE LIST

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