

DABIGATRAN - SAFE PRESCRIBING - NOT A MAGIC BULLET

- ▶ EDUCATE PATIENTS TO REPORT ANY BLEEDING IMMEDIATELY
- ▶ THERE IS NO ANTIDOTE - BLEEDING MAY REQUIRE URGENT REFERRAL
- ▶ CHECK RENAL FUNCTION BEFORE PRESCRIBING - USE CORRECT DOSE
- ▶ CONSIDER POTENTIAL INTERACTIONS AND ADVERSE EFFECTS
- ▶ FUNDED FOR ATRIAL FIBRILLATION (AF) AND PREVENTION OF VENOUS THROMBOEMBOLISM (VTE) AFTER MAJOR ORTHOPAEDIC SURGERY
- ▶ GOOD COMPLIANCE IS VITAL

Dabigatran etexilate is a direct thrombin inhibitor, funded for AF (prevention of stroke, embolism and reduction of vascular mortality) and for prophylaxis of VTE post major orthopaedic surgery^{1,2}.

EDUCATE PATIENTS TO REPORT ANY BLEEDING IMMEDIATELY

Unlike warfarin, dabigatran has a predictable dose-response³, and does not require regular blood testing during treatment¹. However, without the use of reliable monitoring parameters such as the INR for warfarin¹, the bleeding risk of dabigatran may be difficult to manage. An initial assessment using thrombin time (TT) may be helpful to guide dose individualisation but the relationship between TT and bleeding risk for patients on dabigatran is unknown. The activated partial thromboplastin time (aPTT) does not have a linear association with the dose of dabigatran⁴ and may underestimate the level of thrombin inhibition.

As with all anticoagulants, there is a risk of bleeding³. Avoid in patients with haemorrhagic risk factors e.g. gastrointestinal bleeding, recent trauma, stroke (within 6 months) or following brain, spinal or ophthalmic surgery³. Educate patients to report any signs of bleeding immediately.

THERE IS NO ANTIDOTE - BLEEDING MAY REQUIRE URGENT REFERRAL

There is no antidote for dabigatran³, unlike vitamin K for warfarin. Monitor for signs of bleeding at each appointment and be aware of signs of anaemia. **If bleeding**, discontinue dabigatran, check TT and aPTT³ and discuss with a haematologist or cardiologist. A sophisticated combination of measures eg: charcoal, transfusion, haemodialysis⁴ may be required to contain the situation.

CHECK RENAL FUNCTION BEFORE PRESCRIBING - USE CORRECT DOSE

Dabigatran is predominantly cleared by the kidneys, and will accumulate in patients with poor renal function. It **must not** be given to patients with a creatinine clearance (CrCl) of less than 30ml/min³. Discontinue if acute renal failure develops while on treatment³. Older adults with AF and others who have a compromised renal function (CrCl 30-50ml/min), should be prescribed a lower dose³ (see dosing box).

NOTE: It is recommended that prescribers do not rely on the laboratory reported eGFR. Calculate CrCl based on lean body weight (or actual body weight if small) before prescribing, and every 3 months while on treatment⁵. Check more frequently if the patient is likely to be dehydrated, or is prescribed concomitant medicines that will further compromise renal function (e.g. diuretics, NSAIDs).

CONSIDER POTENTIAL INTERACTIONS AND ADVERSE EFFECTS

The major issues with dietary and drug interactions associated with warfarin do not appear to be so prevalent with dabigatran⁶. However, there are still important interactions to be aware of. In particular, combinations with inducers or inhibitors of P-glycoprotein, e.g. ketoconazole and rifampicin should be avoided³. Interactions observed with amiodarone and verapamil are due to an induction of P-glycoprotein in the gut³; this interaction might be minimised by dosing at different times of the day, however this combination is best avoided. There are many other agents with potential interactions which haven't been studied in detail yet, including St John's Wort and carbamazepine; these agents may reduce the efficacy of dabigatran.

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Concomitant clopidogrel and aspirin will increase the risk of bleeding; caution is advised with NSAIDs³. Since regular monitoring is not required, the extent of individual interactions may only become apparent when patients present with bleeding or an embolic event. Please make sure the patient is aware of this and reports any unexplained bruising or bleeding immediately, especially gastrointestinal bleeds.

NOTE: In one of the major clinical trials, there was a higher prevalence of dyspepsia (11%) in the dabigatran arm compared to warfarin (5%); more patients in the dabigatran arm discontinued the study compared to those given warfarin⁷.

ATRIAL FIBRILLATION (AF) INDICATION

Patients with AF require ongoing anticoagulation to reduce the risk of blood clots. These can potentially lead to stroke and systemic embolism. Dabigatran may be a useful alternative for patients with AF who are not managing the monitoring requirements for warfarin, or are not well controlled^{1,8}. Patients who are currently prescribed aspirin instead of warfarin, because of concerns about interactions or managing regular testing, may benefit from dabigatran instead of aspirin. Be aware that the bleeding risk of dabigatran is similar to warfarin¹ and much higher than aspirin alone. If unsure, do not change from warfarin without specialist advice.

NOTE: Dabigatran is not currently licensed for use in patients with mechanical valves or valve disease¹.

PREVENTION OF VENOUS THROMBOEMBOLISM (VTE) INDICATION

Patients undergoing major orthopaedic surgery are at significant risk of VTE. Dabigatran may be considered for patients who need short term prophylaxis **after** orthopaedic surgery³. For this indication, dosing is once daily (see dosing box).

NOTE: Dabigatran is not licensed for the treatment¹ or long term prophylaxis of VTE.

GOOD COMPLIANCE IS VITAL

The peak concentration of dabigatran is reached between 30 minutes and two hours after dosing³. Be aware that there is a rapid loss of effect if doses are missed; good compliance is vital. Take this into account when considering switching patients to dabigatran from warfarin if there are already concerns about compliance. Make sure the patient understands the importance of good compliance.

Due to a rapid loss of chemical stability once opened³, dabigatran must be dispensed in the original pack. It is not suitable for re-packing into compliance aids like Webster[®] or Medico[®] packs. The capsules must be swallowed whole; the contents must not be sprinkled onto food³.

NOTE: If dyspepsia is likely to result in non-compliance, consider alternative anticoagulants.

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DOSING INFORMATION

ATRIAL FIBRILLATION³

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

150mg twice daily

Adults over 80 years* 110mg twice daily

Renal impairment

Moderate renal impairment (CrCl 30-50ml/min)

110mg twice daily⁵

Severe renal impairment (CrCl <30ml/min)

Do not prescribe

PREVENTION OF VTE following major orthopaedic surgery³

Knee replacement surgery

110mg within 1-4 hours of completed surgery, then 220mg once daily for 10 days

Hip replacement surgery

110mg within 1-4 hours of completed surgery, then 220mg once daily for 28-35 days

Renal impairment

Moderate renal impairment (CrCl 30-50ml/min)

150mg once daily

Severe renal impairment (CrCl <30ml/min)

Do not prescribe

*Due to an expected age-related decline in renal function

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NOTE: The majority of dosing data is for patients weighing between 50 and 100kg³.

There is currently no information on dosing or safety in those under 18 years, in pregnancy or lactation³.

Enoxaparin should still be used for VTE in pregnancy, and warfarin remains the treatment of choice when breastfeeding.

For further information on other high-risk medicines visit our website at: www.saferx.co.nz

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DISCLAIMER: This information is provided to assist primary care health professionals with the use of prescribed medicines. Users of this information must always consider current best practice and use their clinical judgement with each patient. This information is not a substitute for individual clinical decision making. Issued by the Quality Use of Medicines Team at Waitemata District Health Board, email: feedback@saferx.co.nz