

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; Educate 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 be increased with:

- Patients over 75 years old
- Patients with moderate renal impairment (Creatinine clearance (CrCl) 30-50mL/min)
- Concomitant treatment with antiplatelet agents
- Previous gastro-intestinal bleed

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

BLEEDING MAY REQUIRE URGENT REFERRAL

Monitor 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 further with a haematologist or cardiologist. A combination of intensive interventions may be required to contain the situation. A dabigatran reversal agent called idarucizumab (Praxbind[®]) is available in the hospital setting for patients requiring urgent reversal for bleeding 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 will 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, ticagrelor, 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

2

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 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 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 of administration varies depending on the 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

- 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)
- Medsafe Safety Information. Update on Pradaxa (dabigatran etexilate). 2013 www.medsafe.govt.nz/consumers/Safety-of-Medicines/UpdateOnPradaxa.asp (Accessed 15-10-14)
- New Zealand Formulary, dabigatran. http://nzf.org.nz/nzf_1502.html?searchterm=dabigatran (Accessed 14-10-14)

DOSING INFORMATION

ATRIAL FIBRILLATION³ (Prevention of stroke, systemic embolism and reduction of vascular mortality)

Age	Dose
18-79y	150mg twice daily
75-80y (if low thromboembolic risk and high bleeding risk)	110mg twice daily
80y and older	110mg twice daily

Renal impairment	Dose
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:	Dose
1-4 hours following surgery	110mg
Days 2-10 postoperatively	220mg once daily

Hip replacement surgery:	Dose
1-4 hours following surgery	110mg
Days 2-28 or 2-35 postoperatively	220mg once daily

Renal impairment:	Dose
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
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Renal impairment:	Dose
Severe (CrCl <30mL/min)	do not prescribe

TREATMENT OF VTE

Following parenteral anticoagulant for at least 5 days	150mg twice daily (up to 6months)
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Renal impairment	Dose
Severe (CrCl <30mL/min)	do not prescribe

Note: The majority of dosing data is for patients weighing between 50 and 100kg.³ There is currently no information about safe dosing for patients under 18 years, or during pregnancy or lactation.³ Enoxaparin should still be used for VTE in pregnancy, and warfarin remains the treatment of choice when breastfeeding.

[CLICK HERE FOR FURTHER INFORMATION ON DABIGATRAN AND A FULL REFERENCE LIST](#)

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

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