DABIGATRAN (PRADAXA®)

GUIDELINES FOR ANTICOAGULATION UPDATED JULY 2017

This guideline provides a summary of the inpatient management of **adult** (over the age of 18) patients receiving DABIGATRAN.

This guideline should be used in conjunction with Therapeutic Goods Administration (TGA) approved Product Information (PI), Clinical Excellence Commission (CEC) Non-Vitamin K Antagonist Oral Anticoagulant (NOAC) Guidelines and specialist advice.

Commencing treatment:

Conduct the following prior to commencing treatment:

- Full blood count (FBC)
- Prothrombin time (PT)
- Activated Partial Thromboplastin Time (aPTT)
- Liver Function Test (LFT)
- Renal function - estimated creatinine clearance (CrCl) should be calculated using the Cockcroft-Gault equation (do not use eGFR reported in pathology results). Ideal body weight should be used for calculating estimated creatinine clearance in patients who are overweight or obese. For all other patients use actual body weight.

Further investigate if results are found to be abnormal.

Review the following:

Contraindications to therapy, drug and antithrombotic interactions, and administration considerations.

Contraindications to therapy:

- Known hypersensitivity
- Creatinine clearance <30mL/min
- Clinically significant active bleeding
- Significant inherited or acquired bleeding disorder
- Hepatic disease with coagulopathy (Child-Pugh C)
- Organ lesions at risk of bleeding including intracranial haemorrhage in previous 6 months
- Indwelling spinal or epidural catheter and during the first six hours after removal
- Mechanical heart valve
- Pregnancy or breastfeeding mother.

Caution:

In patients with any history of gastrointestinal bleeding use DABIGATRAN with caution and seek advice.

DABIGATRAN (Pradaxa®) 110 mg capsule

DABIGATRAN (Pradaxa®) 150 mg capsule

75 mg (white) capsule also available.
Images courtesy of Boehringer Ingelheim Pty. Ltd. Images not to scale.

Drug Interactions[1]

Class or medicine (Not an exhaustive list)	Advice
Amiodarone	Caution
Anticonvulsants *phenytoin, carbamazepine*	Caution
Azole antifungals *e.g. itraconazole voriconazole, posaconazole*	Contraindicated
Dronedarone	Contraindicated
Fluconazole	Caution
Immunosuppressants (Calcineurin inhibitors) *e.g. cyclosporin, tacrolimus*	Contraindicated
Macrolides *e.g. clarithromycin, erythromycin*	Caution
SSRI* / SNRI** *e.g. escitalopram, sertraline, venlafaxine*	Caution
Rifampicin	Caution
Verapamil	Relative contraindication Refer to PI or AMH

**Selective serotonin re-uptake inhibitor (SSRI), **Serotonin norepinephrine re-uptake inhibitor (SNRI)*

Antithrombotic interactions[1]

Action	Example (Not an exhaustive list)	Advice
Antiplatelet	NSAIDS Aspirin Clopidogrel Prasugrel Dipyridamole	Caution
	Ticagrelor	Relative contraindication
	Dual-antiplatelets	Relative contraindication
Anticoagulant	Warfarin Enoxaparin Heparin	Contraindicated *(unless transitioning between anticoagulants)*

Administration considerations/ instructions:

- Capsules must not be opened – **Not suitable for patients unable to swallow a capsule whole**
- Capsules must not be removed from packaging until the time of administration – **Not suitable for dose administration aids (e.g. Webster-pak®).**

DABIGATRAN dosing[1]

Indication	Risk factors*	Dose	Duration
Prevention of stroke and systemic embolism in non-valvular AF in patients with at least ***one*** of the following risk factors: • prior stroke, TIA or non-central nervous system systemic embolism; • age ≥75 years, • hypertension, • diabetes mellitus or • heart failure and/ or left ventricular ejection fraction ≤35%	Patient with at least ***one*** of the following risk factors: • Age ≥75 years; ***or*** • CrCl 30 - 50 mL/min; ***or*** • high bleeding risk (consider HAS BLED score)	DABIGATRAN 110 mg twice daily	Indefinite duration
	Patient with: • Age <75 years; ***and*** • CrCl >50 mL/min; ***and*** • no bleeding risk (consider HAS BLED score)	DABIGATRAN 150 mg twice daily	Indefinite duration
Prevention of VTE after elective**: • Total hip replacement (THR) ***or*** • Total knee replacement (TKR)	Patient with: CrCl 30 – 50 mL/min	DABIGATRAN 150 mg once daily	THR = 28 – 35 days TKR = 10 days
	Patient with: CrCl >50 mL/min	DABIGATRAN 220 mg once daily	THR = 28 – 35 days TKR = 10 days
Treatment and prevention of recurrent DVT and/or PE	At the time of publication, DABIGATRAN was not listed with the PBS for this indication Refer to PI or CEC NOAC Guidelines for dosing and further information for this indication		
*DABIGATRAN is contraindicated in patients with CrCl <30mL/min			

***Dabigatran should be initiated within 1-4 hours of completed surgery with a single capsule (110 mg). If haemostasis is not secured, initiation of treatment should be delayed. If treatment is not started on the day of surgery then treatment should be initiated as per above table. For patients who have had an epidural or spinal anaesthesia, see CEC NOAC Guidelines Section 6.1.*

Perioperative management

- A recent CrCl result should be available.
- For urgent or high bleeding risk elective surgery check: estimated CrCl, FBC, PT, aPTT and TT. Consider DABIGATRAN level (where available).
- Refer to CEC NOAC Guidelines for advice on spinal and epidural anaesthesia, or patients undergoing a lumbar puncture.

Timing of ceasing DABIGATRAN prior to surgery[1]

DABIGATRAN	Minimal bleeding risk procedures*	Low bleeding risk procedures*	High bleeding risk procedures*
Normal renal function (CrCl ≥80 mL/min)	Withholding DABIGATRAN may not be required	Last dose 24 hours before surgery	Last dose 48 hours before surgery
Mildly impaired renal function (CrCl 50-79 mL/min)	Withholding DABIGATRAN may not be required	Last dose 24 – 48 hours before surgery	Last dose 48 – 72 hours before surgery
Moderately impaired renal function (CrCl 30-49 mL/min)	Withholding DABIGATRAN may not be required	Last dose 48 – 72 hours before surgery	Last dose 96 hours (4 days) before surgery
CrCl <30 mL/min		SEEK SPECIALIST ADVICE. Stop at least 5 days before high-risk surgery	

**Refer to CEC NOAC Guidelines for information on minimal, low and high bleeding risk procedures.*

Recommencing NOAC post-operatively[2]

Low bleeding risk procedure

- Start or resume 24 hours after surgery

High bleeding risk procedure

- Do not start or resume therapeutic dosing until 48 – 72 hours after surgery
- Consider alternative VTE prophylaxis post-operatively

THR and TKR prophylaxis with NOAC may be recommenced 24 hours after surgery.

Managing Bleeding

Mild bleeding:

- Establish dose and last time taken
- Initiate standard resuscitation procedures
- Consider: FBC, group and hold, CrCl, APTT, TT, DABIGATRAN level (where available)
- Establish if taking any other medicines with antithrombotic action
- Seek advice from a senior medical officer whether to delay dose or discontinue
- Refer to CEC NOAC Guidelines.

Clinically significant or life-threatening bleeding:

- As above
- Consult haematologist
- Refer to CEC NOAC Guidelines [Idarucizumab (DABIGATRAN reversal agent) is available in Australia. Check for local availability].

References: 1.Boehringer Ingelheim Pty Limited. Product Information Pradaxa® (dabigatran etexilate). Therapeutic Goods Administration Website [updated 28 February 2017], 2.Tran H, Joseph J, Young L, McRae S, Curnow J, Nandurker H, et al. New oral anticoagulants: a practical guide on prescription, laboratory testing and peri-procedural/bleeding management Internal Medicine Journal 2014;44:525-36

Dabigtran (Pradaxa®) Guidelines for Anticoagulation Updated July 2017. Released September 2017.

MEDICATION SAFETY AND QUALITY High-Risk Medicines

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