Dabigatran [Pradaxa®] – Specialist Advised Drug Checklist

Indication: Stroke and systemic embolism prevention in AF and treatment/ secondary prevention of DVT/PE in adults 18 years plus

Coventry & Warwickshire Area Prescribing Committee

Affix patient identification label in box below or complete details

Surname	Patient i.d.No.
Forename	D.O.B. DDMMYYYY
Address	NHS No.
	Sex. Male / Female
Postcode	

The Area Prescribing Committee requires healthcare professionals, prior to initiation, to complete this assessment of suitability and also refer to the patient's usual anticoagulation clinic for further counselling and provide contact details in the event of bleeding / need advice.

Use in conjunction with DOACs comparison charts (DCC04a & DCC04b)

Overview[1,2]

Dabigatran is NICE approved as an option for anticoagulation in Atrial Fibrillation (AF) and Venous Thromboembolism *i.e. Deep Vein Thrombosis and Pulmonary Embolism* (DVT/PE). Contraindications include; any form of prosthetic heart valve / severe renal impairment / pregnancy / certain concomitant medications - refer to BNF for further details. It is also not recommended in patients with active cancer or undergoing anticancer treatment (treat with low molecular weight heparins (LMWH)), or in patients with a recent history of peptic ulcer disease or Gastrointestinal (GI) tract bleeding.

Dabigatran offers many potential advantages over warfarin e.*g.* relatively few interactions and no need for coagulation monitoring, although bleeding rates are similar. In common with most of the other direct oral anticoagulants (DOACs), there is no currently licensed or approved antidote. Dabigatran may accumulate in renal and hepatic failure. Renal function can decline asymptomatically - monitoring annually is recommended.

Information relating to completion of checklist – see page 3

Renal Function (calculation of creatinine clearance)

It is essential to calculate the patient's true creatinine clearance prior to initiating DOACs

Cockcroft and Gault method provides the most accurate estimate:
Male patients: CrCl (ml/min) = [140 – age (in years)] x weight (in kg) x 1.23 / serum creatinine (in micromol/l)

Female patients: CrCl (ml/min) = [140 – age (in years)] x weight (in kg) x 1.04 / serum creatinine (in micromol/l)

Note: Weight in kilograms (use ideal body weight where fat is likely to be the major contributor to body mass)

Online Cockcroft Gault calculator which may be found at https://www.mdcalc.com/creatinine-clearance-cockcroft-gault-equation or https://www.kidney.org/professionals/KDOQI/gfr_calculatorCoc (Note - SCr (serum creatinine) = mg/dL

Dose recommendations: Standard dose is 150 mg twice daily (if CrCL 15-49ml/min)
DVT/PE - Only start dabigatran following initial use of LMWH for at least 5 days. Dabigatran and initial LMWH should not be administered simultaneously.
Reduced dose: **110 mg twice daily** is recommended in patients aged >80 years or on verapamil.
Reduced dose i.e. **110 mg twice daily** should also be considered in moderate renal impairment e.g. CrCL 30-50mL/min, and/or when additional bleeding risk factors are present e.g. age 75 - 80 years, gastritis, oesophagitis.

Duration of treatment for DVT/PE - Patients with proximal DVT or PE should be treated for at least 3 months. Long term treatment will be considered for recurrent thrombosis, patients with an on-going risk factor, or unprovoked proximal DVT or PE. For many patients (e.g. those with a first unprovoked proximal DVT or PE), a further review will be needed at three months to decide whether or not to stop anticoagulation, and the need for further tests to identify any underlying cause for VTE. This will be arranged at the point of discharge following initial diagnosis, with the specialist as appropriate.

In event of concerns with initiation/management of anticoagulation with Dabigatran suggest refer to local anticoagulation service lead(UHCW or SWFT) or responsible GP in primary care led service.

DO NOT DOSE REDUCE unless instructed by the Summary of Product Characteristics (SPC). Dose reductions are likely to increase the risk of a thrombotic event as the medication will be subtherapeutic. Seek advice if considering a dose reduction as this may increase the risk of harm to the patient.

Missed doses – A forgotten dabigatran dose may still be taken up to 6 hours prior to the next scheduled dose. From 6 hours prior to the next scheduled dose onwards, the missed dose should be omitted. No double dose should be taken to make up for missed individual doses.

Converting from Vitamin K Antagonists (VKA) e.g. warfarin
Warfarin treatment should be stopped and dabigatran should be initiated when the INR is ≤ 2.0
If patients are switching from warfarin, commence dabigatran when INR < 2.

Assessment of stroke and bleeding risks for patients with NVAF (as per the NICE guideline)

Stroke risk: Use the **CHA_2DS_2-VASc** stroke risk score to assess stroke risk in people with any of the following:

1. symptomatic or asymptomatic paroxysmal, persistent or permanent atrial fibrillation
2. atrial flutter
3. a continuing risk of arrhythmia recurrence after cardioversion back to sinus rhythm.

(see http://resources.hrsonline.org/chads2-vasc-calculator.html) or https://www.chadsvasc.org/

Point Scoring:
Congestive heart failure (or Left Ventricular Dysfunction) – **1 point**
Hypertension – **1 point**
Age >75 years – **2 points**
Diabetes – **1 point**
Prior stroke or TIA or thromboembolism – **2 points**
Vascular Disease (previous MI, peripheral arterial disease or aortic plaque) – **1 point**
Age 65-74 Years – **1 point**
Sex Category (Female) – **1 point**

One recommendation suggests a 0 score is **"low"** risk and may not require anticoagulation; a 1 score is **"low-moderate"** risk and should consider anticoagulation, and score 2 or greater is "**moderate-high"** risk and should otherwise be an anticoagulation candidate.

Bleeding risk *(as per the NICE Atrial Fibrillation guideline)* - Use the HAS-BLED score to assess the risk of bleeding in people who are starting or have started anticoagulation.

Offer modification and monitoring of the following risk factors:
- uncontrolled hypertension
- poor control of international normalised ratio (INR) ('labile INRs')
- concurrent medication, for example concomitant use of aspirin or a non-steroidal anti-inflammatory drug (NSAID)
- harmful alcohol consumption.

HAS-BLED Major Bleeding Risk Score[4]

	Clinical Characteristic	Points
H	Hypertension	1
A	Abnormal liver &/or renal function	1 or 2
S	Stroke	1
B	Bleeding diatheses	1
L	Labile INR	1
E	Elderly	1
D	Drugs / Alcohol	1 or 2
	Add points to get score	*

HAS-BLED score	Major Bleed Risk (% per year)[4]
0	1.13
1	1.02
2	1.88
3	3.74
4	8.70
5 to 9	Insufficient data

**HAS-BLED Notes:*
Hypertension: systolic blood pressure >160 mm Hg.
Renal function: creatinine >200 or dialysis.
Liver function: chronic liver disease (eg. cirrhosis) **or** bilirubin >2x ULN +AST /ALP >3x upper limit normal).
Bleeding: previous bleeding, bleeding diathesis or unexplained anaemia.
Labile INRs: Time in Treatment Range <60%.
Drugs: concomitant use of drugs, e.g. antiplatelet agents and non-steroidal anti-inflammatory drugs.
Alcohol: excess alcohol

Low risk = 0-2 and **high risk** = ≥ 3 (high risk suggests caution required and more frequent reviews are recommended)

References:
1. Summary of Product Characteristics (SPC). Available at www.medicines.org.uk Last updated 7th June 2018
2. MHRA Drug safety update Vol 5 Issue 5, Dec 2011: A2
3. NICE TA249 (Mar 2012) Dabigatran etexilate for the prevention of stroke and systemic embolism in atrial fibrillation
4. NICE TA327 (Dec 2014) Dabigatran etexilate for the treatment and secondary prevention of deep vein thrombosis and/or pulmonary embolism

Please ensure all sections of the checklist on page 3 are completed: ⟶

Confirm indications *please tick as appropriate →*	**Yes**	**No**
1. Non-Valvular Atrial Fibrillation (NVAF) with one or more of the following risk factors		
1a. Congestive heart failure		
1b. Hypertension		
1c. Age ≥ 75 years		
1d. Diabetes Mellitus		
1e. Prior stroke or transient Ischaemic attack (TIA)		
2. DVT treatment or prevention of recurrent DVT		
3. PE treatment or prevention of recurrent PE		

Stroke and bleeding risks assessment (for patients with NVAF) - *see info on page 1*		
1. Stroke risk: CHA_2DS_2-VASc score (*maximum score out of 10)*	enter score number/10 →	
2. Bleeding risk: HAS-BLED score *(maximum score out of 9)*	enter score number/9 →	

Confirm no contraindications *tick or add notes on completion*	**Tick**	**Notes**
1. Confirm body weight between 40kg - 120kg (unless directed by haematology after measurement of drug specific levels in patients <40kg & >120kg) add weight in kg		
2. Ensure adequate renal function, Creatinine Clearance (CrCL) >15 mL/min. DOACs are contraindicated in patients on renal replacement therapy such as dialysis.- *see renal function calculator on page 1* State dose and frequency		
3. Review patient for any contraindicated medication & action - *e.g.* Azole-antimycotics, HIV protease Inhibitors - e.g. ritonavir) & Dronedarone - *please refer to BNF / manufacturer's datasheet for further examples*		
4. Check patient is not pregnant or breastfeeding.		
5. Ensure that there is no history of severe liver disease (Child Pugh grade B or C).		
6. Review any contraindications to anticoagulation *e.g.* bleeding. *Consider alternative anticoagulant if recent history of Dyspepsia or peptic ulcer disease/GI bleeding (dabigatran is associated with an increased risk of Dyspepsia and GI bleeding compared with warfarin).*		
7. Review cardiac history – not recommended in known haemodynamically significant valvular heart disease or with prosthetic heart valves (tissue or mechanical).		

General Assessment / Informed consent / patient counselling *tick or add notes on completion*		**Tick**	**Notes**
1. Ensure patient understands the importance of adherence to medication dosing. *N.B. Due to the short half-life of dabigatran compared to warfarin erratic compliance could result in reduced anticoagulation efficacy*			
2. Review baseline bloods are all Satisfactory: Full Blood Count (FBC) Liver Function Tests (LFTs) Urea and Electrolytes (U&Es)	**Not recommended if;** ➢ Platelets <70 x10^9/l (If platelets between 50 to 70 x 10^9, consider discussion with haematologist as benefits of anticoagulation may outweigh bleeding risks) ➢ CrCL: <15mL/min ➢ LFT: Liver enzymes elevated >2x normal ➢ Coagulation Screen: APTT >1.5x normal; INR >1.4 - standard coagulation tests *e.g.* PT/APTT/INR should not be measured or used for monitoring drug effect as they are not predictable and do not correlate with circulating levels of drug.		
3. **At patient review** check the following: patient's body weight; recalculate renal function: **annually** if CrCl >60ml/min, **6 monthly** if 45 - <60ml/min, **3 monthly** if 30 - <45ml/min or **HAS-BLED score ≥ 3;** drug interactions; recalculate HASBLED score; LFTs and FBC.			
4. Explain purpose of anticoagulation with dabigatran: avoidance of embolic stroke/peripheral embolisation secondary to atrial fibrillation **OR** treatment/prevention of DVT/PE. Issue patient booklet and alert card **click here for AF** or use manufacturer's alert card and booklet			
5. Explain side effects - **seek urgent medical attention if develops severe bleeding** e.g. blood in faeces, vomit or sputum, vaginal bleeding (other than regular period), nose bleeds, severe & spontaneous bruises and **severe unusual headache** (particularly if following head trauma associated with features of concussion). *There is a direct antidote to Dabigatran, Praxbind® (idarucizumab) that can be considered. In the event of life threatening bleeding or need for emergency surgery stop rivaroxaban - anticoagulant effect will wear off after approximately 24 - 48 hours post last dose. There are interventions available in hospital that may reduce the anticoagulant effect, in case of life threatening bleed. (consider urgent haematology opinion).*			
6. **Explain how to take** - The capsules can be taken with or without food and should be swallowed as a whole with a glass of water, to facilitate delivery to the stomach. Patients should be instructed not to open the capsule as this may increase the risk of bleeding.			
7. **Explain to patient to inform medical staff** that they are taking dabigatran if prescribed new medications or planning to undergo surgery/invasive procedures (including dental extractions. *Bleeding risk if started immediately post op in view of short half-life. If the patient has had a stent/Percutaneous Intervention (PCI) / Coronary Artery Bypass Graft (CABG), review aspirin and/or clopidogrel duration and need to continue, with cardiology / as per cardiology advice.*			

Print Name: _____ Signature: _____ Position: _____

Contact details: _____ (tel, email) Date: _____