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Anticoagulation for non-valvular atrial fibrillation (NVAF)

Frimley Health and Care

Offer anticoagulation if CHA2DS2VASc ≥2 (consider anticoagulation if score = 1 in males). Shared decision to be made with the individual about whether to start anticoagulation and about how to reduce modifiable risk factors for bleeds. Using a bleed risk tool may help inform shared decision making e.g. ORBIT bleed risk tool.

Before initiation of any anticoagulation the following baseline parameters should be checked: Weight, FBC, U&Es, LFTs, Clotting screen & INR (If INR ≥ 1.4 discuss with haematology before starting oral anticoagulation)

Is anticoagulation with warfarin mandated? (mechanical heart valves, moderate - severe mitral stenosis, antiphospholipid syndrome)

Yes → Initiate warfarin with appropriate INR monitoring. A higher INR target may be required if mechanical heart valve / antiphospholipid syndrome

No

Does the patient have a CrCl <15ml/min or are they on dialysis?

Yes → Consider the risks and benefits with the patient in severe renal dysfunction where bleeding risk is elevated. Consider initiating warfarin with INR range 2.0-3.0

No

Does the patient have any two of the following characteristics: age ≥ 80 years, body weight ≤ 60 kg, or serum creatinine ≥ 1.5 mg/dL (133 micromole/L)

Yes → Commence reduced dose of apixaban 2.5mg twice daily

No

Commence apixaban 5mg twice daily

Rivaroxaban is on the formulary and is first line choice if a once daily DOAC is needed. If patient already switched from another DOAC to edoxaban, patient can remain on this

If CrCl ≥ 95ml./min consider apixaban, rivaroxaban or dabigatran.

DOACs should be used first line for NVAF. Exclusions include:

- Mechanical heart valves (or within 3 months of a bioprosthetic (tissue) valve)
- Moderate to severe mitral valve stenosis
- Antiphospholipid syndrome (APS)
- Renal failure with creatinine clearance < 15mls/min
- Patient requiring a higher INR range (>2-3)
- Concomitant use of drugs which are contraindicated with DOACs– see SmPCs
- Bodyweight >120kg or BMI>40 (bodyweight <50kg use DOACs with caution)
- LFT's - ALT/AST >2 x Upper Limit of Normal (ULN) or Bilirubin > 1.5x ULN

DOAC monitoring

FBC, LFTs and weight annually.

Recommended renal monitoring frequencies:

- Creatinine Clearance >60mls/min. Check U&E and CrCl every 12 months
- Creatinine Clearance 30-60mls/min. Check U&E and CrCl every 6 months
- Creatinine Clearance 15-30ml/min. Check U&E and CrCl every 3 months

Creatinine Clearance ≤15mls/min

When creatinine clearance has fallen to <15mls/min, DOAC should be discontinued. Warfarin can be used in those with poor renal function following appropriate discussion regarding stroke and bleeding risk. Alternatively a left atrial appendage occlusion (LAAO) device could be considered in line with NICE guidance.

LAAO

If a patient has significant risk of AF related cardioembolic stroke but cannot receive an oral anticoagulant either due to renal function or bleeding consider referral to cardiology for consideration of LAAO device insertion.

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Information on switching from warfarin to a DOAC

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It is for the prescribing clinician to determine which DOAC(s) are clinically appropriate for an individual patient based upon the relevant NICE technology appraisal guidance.

When switching to a DOAC, care should be taken to follow the recommendations in the relevant SPC:

- Apixaban Search Results - (emc) (medicines.org.uk)
- Dabigatran Search Results - (emc) (medicines.org.uk)
- Edoxaban Search Results - (emc) (medicines.org.uk)
- Rivaroxaban Search Results - (emc) (medicines.org.uk)

A switch from warfarin to a DOAC should not be considered for patients:

- With a prosthetic mechanical valve
- With moderate to severe mitral stenosis
- With antiphospholipid antibody syndrome (APS) (except where advised by an Haematology specialist)
- Who are pregnant breast-feeding or planning a pregnancy
- Requiring a higher INR than the standard INR range of 2.0 – 3.0
- With severe renal impairment - Creatinine Clearance (CrCl) < 15ml/min
- With venous thrombosis at unusual sites (e.g. portal vein thrombosis)
- If LFTs - ALT/AST >2 x ULN & Bilirubin > 1.5 x ULN

Seek advice for patients with:

- Active malignancy/ chemotherapy
- Prescribed interacting drugs – check SmPCs for full list
- Some HIV antiretrovirals and hepatitis antivirals - check with HIV drug interactions website at https://www.hiv-druginteractions.org/
- Some antiepileptics- phenytoin, carbamazepine, phenobarbitone or rifampicin are likely to reduce DOAC levels so should be discussed with an anticoagulation specialist
- Extremes of bodyweight: > 120kg (or BMI > 40) or < 50kg
- On triple therapy (dual antiplatelet therapy plus anticoagulant)

Suggested process for each individual:

1. Check recent U&Es, LFTs and FBC (ideally within the last 3 months) and calculate creatinine clearance (CrCl) (https://www.mdcalc.com/creatinine-clearance-cockcroftgault-equation) using actual body weight from last 12 months.

2. Check INR.

3. Discuss options with your patient and/or carers (as appropriate) and, with consent, prescribe DOAC at appropriate dose – apixaban or rivaroxaban preferred first-line: see page 1.

4. Remove warfarin from the repeat prescription after initiating DOAC.

5. SmPCs for individual DOACs recommend different INR thresholds for starting DOACs after stopping warfarin. The EHRA gives pragmatic guidance and recommends that the INR should be < 2.5 when the DOAC is started.

- If INR < 2: Commence DOAC that day
- If INR between 2 and 2.5: Commence DOAC the next day ideally (or the same day)
- If INR between 2.5 and 3: Withhold warfarin for 24-72 hours and then initiate DOAC

https://academic.oup.com/eurheartj/article/39/16/1330/4942493?guestAccessKey=

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6. Provide written instructions and involve family members / carers where possible to minimise the risk of patients taking both warfarin and the DOAC concurrently. Particular care should be taken where patients are using medication compliance aids to minimise the risk of incorrect dosing. Ask patient / carers to return any warfarin to the community pharmacy for disposal.

7. Provide an up-to-date Anticoagulant Alert card and DOAC counselling (see checklist).

8. Where the switch to a DOAC is undertaken outside the GP practice, provide accurate information relating to indication, baseline tests and monitoring requirements to allow primary care to safely take over prescribing responsibility.

9. Inform community nursing teams if they have been monitoring INR or administering warfarin.

10. Ensure appropriate on-going monitoring is in place using the clinical system recall function – frequency will depend on renal function, age and frailty.

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Counselling checklist for DOACs

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Counselling points	Sign
Shared decision making considering the risks and benefits of anticoagulants. Patient decision aid **available here**	
Explanation of an anticoagulant (increases clotting time and reduces risk of clot formation) and explanation of indication for therapy	
Differences between DOAC and warfarin (if applicable for patients converting from warfarin to DOAC therapy or offering choice of anticoagulation agent)	
• No routine INR monitoring	
• Fixed dosing	
• No dietary restrictions and alcohol intake permitted (within national guidelines)	
• Fewer drug interactions	
Name of drug: generic & brand name	
Explanation of dose: strength & frequency	
Duration of therapy: indefinitely for AF	
To take with food (dabigatran and rivaroxaban). Not required for apixaban or edoxaban	
Missed doses:	
• Edoxaban and rivaroxaban can be taken within 12 hours of missed dose, otherwise omit the missed dose	
• Apixaban and dabigatran can be taken within 6 hours of missed dose, otherwise omit the missed dose	
Extra doses taken: obtain advice from pharmacist/GP/NHS 111	
Importance of adherence: short half-life and associated risk of stroke and/or thrombosis if non-compliant	

Counselling points	Sign
Common and serious side-effects and who/when to refer: symptoms of bleeding/unexplained bruising. Avoidance of contact sports.	
• Single/self-terminating bleeding episode – routine appointment with GP/pharmacist	
• Prolonged/recurrent/severe bleeding/head injury – A&E	
• Major bleeds managed/reversed by supportive measures, Prothrombin, Complex Concentrate (PCC), and availability of antidote	
Drug interactions and concomitant medication: avoid NSAID's. Always check with a pharmacist regarding. OTC/herbal/ complimentary medicines	
Inform all healthcare professionals of DOAC therapy: GP, nurse, dentist, pharmacist i.e. prior to surgery	
Pregnancy and breastfeeding: potential risk to foetus – obtain medical advice as soon as possible if pregnant/considering pregnancy. Avoid in breastfeeding	
Storage: dabigatran must be kept in original packaging – moisture sensitive. All other DOAC are suitable for standard medication compliance aids/ dosette boxes if required	
Follow-up appointments, blood tests, and repeat prescriptions: where and when	
Issue relevant patient information AF booklet/leaflet and anticoagulant patient alert card	
Give patient opportunity to ask questions and encourage follow up with community pharmacist (NMS – New Medicine Service)	

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DOAC Prescribing for Non-Valvular AF (NVAF)

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DOAC	Apixaban	Rivaroxaban	Edoxaban	Dabigatran
Dosing in Non-valvular AF (lifelong unless risk: benefit of anticoagulation therapy changes)	Prescribe Apixaban 5mg twice daily Reduce dose to 2.5mg twice daily if at least two of the following characteristics: age ≥ 80 years, body weight ≤ 60 kg, or serum creatinine ≥ 133 micromol/l or if exclusive criteria of CrCl 15 - 29 ml/min.	Prescribe Rivaroxaban 20mg once daily Reduce dose to 15mg once daily if CrCl< 50mL/min in NVAF patients only.	Prescribe Edoxaban 60mg once daily Reduce dose to 30mg once daily if: Body weight <61kg, or CrCl< 50ml/min, or co-prescribed with ciclosporin, dronedarone, erythromycin or ketoconazole.	Prescribe Dabigatran 150mg twice daily if aged <75 years, CrCl> 50mL/min, low risk of bleeding (weight <50kg with close clinical surveillance) Reduce dose to 110mg twice daily if aged > 80 years or prescribed verapamil. Consider 110mg twice daily based on individual assessment of thrombotic risk and the risk of bleeding in patients aged between 75 and 80 years or with CrCl <50mL/min or with increased risk of bleeding (including gastritis, oesophagitis, gastro-oesophageal reflux).
Contraindicated / Not recommended	CrCl <15ml/min	CrCl <15ml/min	CrCl <15ml/min	CrCl <30ml/min
Cautions **See also individual SPCSs**		CrCl <30ml/min. Take with or after food (15mg and 20mg doses).	CrCl >95ml/min	Do not use in a standard medication compliance aids (MCA)
Interactions **Check BNF:** **www.bnf.org SPC:** **www.medicines.org.uk**	Ketoconazole, itraconazole, voriconazole, posaconazole, ritonavir - not recommended (See SPC for full details) Rifampicin, phenytoin, carbamazepine, phenobarbital, St. John's Wort – use with caution. Do not use apixaban with patients on strong enzyme inducers for acute VTE treatment	Ketoconazole, itraconazole, voriconazole, posaconazole, ritonavir, dronedarone – not recommended (See SPC for full details) Rifampicin, phenytoin, carbamazepine, phenobarbital, St. John's Wort – Should be avoided.	Rifampicin, phenytoin, carbamazepine, phenobarbital or St. John's Wort – use with caution Ciclosporin, dronedarone, erythromycin, ketoconazole – reduce dose as above. (See BNF and SPC for edoxaban for further information)	Ketoconazole, ciclosporin, itraconazole, tacrolimus, dronedarone - contraindicated (See SPC for full details) Rifampicin, St John's Wort, carbamazepine, phenytoin –should be avoided. Amiodarone, quinidine, ticagrelor, posaconazole – use with caution. Verapamil (use reduced dose). Antidepressants: SSRIs and SNRIs– increased bleeding risk
Nasogastric administration/ crushing & dispersing	Yes	Yes	Yes	No