City & Hackney guide to DOAC initiation and monitoring in non-valvular AF in primary care

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City & Hackney GP Confederation
A community interest company

Which patients?

1. Indication for anticoagulation:

- Non-Valvular AF/Atrial Flutter
- CHA_2DS_2-VASc ≥2 (consider ≥1 for men). *See appendix 1*

2. Contraindications to DOAC:

- Mechanical valve (or within 3 months of a tissue valve)
- Moderate to severe mitral stenosis
- Antiphospholipid syndrome*
- Higher INR range (>2-3)

*Unless discussed with Haematology

3. Assess renal function:

CrCl using actual body weight: https://www.mdcalc.com/creatinine-clearance-cockcroft-gault-equation

- DOACs contraindicated in CrCl <15 ml/min

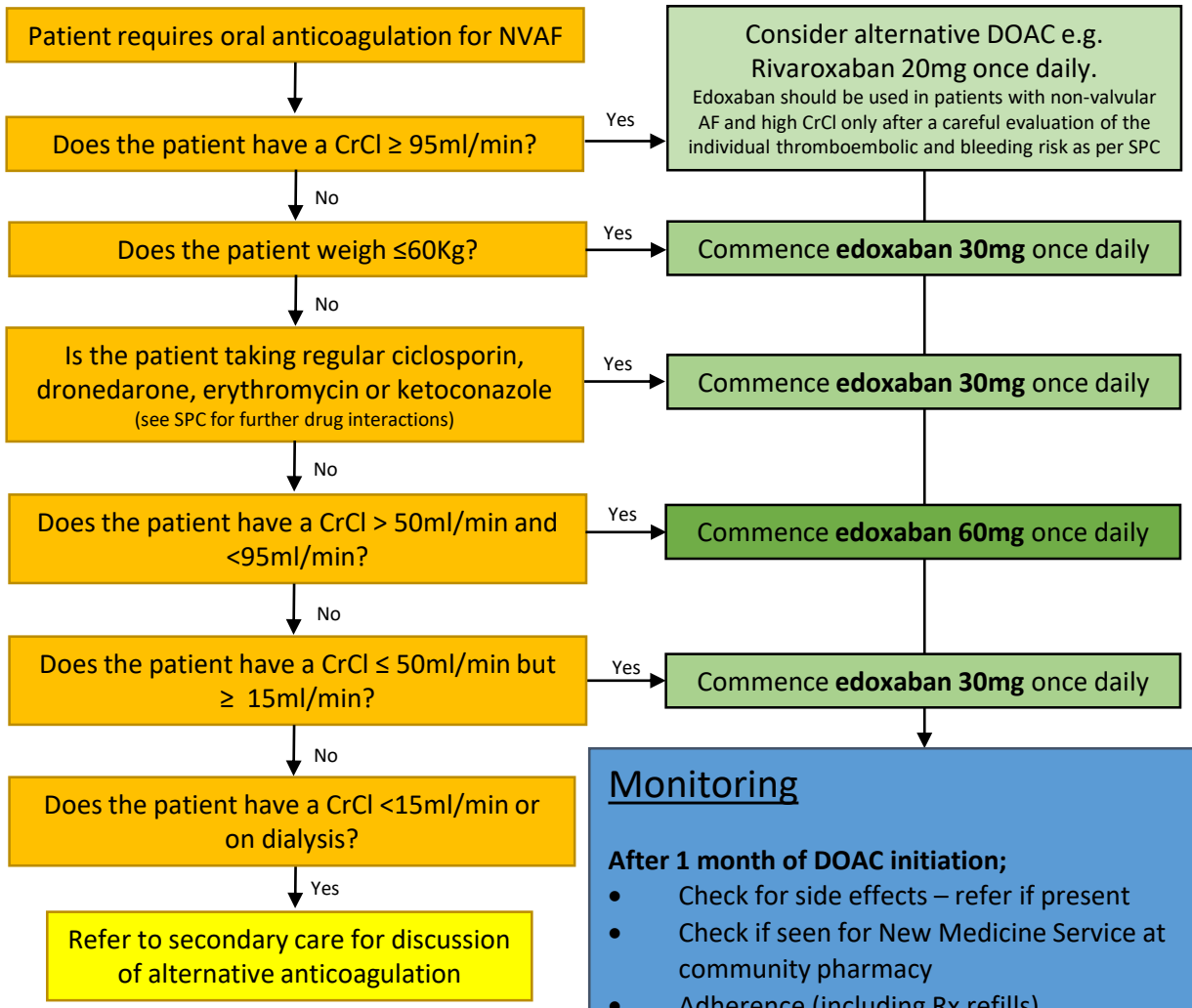
4. Calculate ORBIT score*: https://www.mdcalc.com/calc/10227/orbit-bleeding-risk-score-atrial-fibrillation

*high ORBIT score is not a sole reason to withhold anticoagulation. *See appendix 2*

Data	Result	Action	When to refer
CHA_2DS_2-VASc score https://www.mdcalc.com/cha2ds2-vasc-score-atrial-fibrillation-stroke-risk		≥2 (or ≥1 men) eligible for anticoagulation For DCCV any score	
Calculate ORBIT score: https://www.mdcalc.com/calc/10227/orbit-bleeding-risk-score-atrial-fibrillation		Modify risk factors to reduce bleeding risk	GI/GU bleed within 3/12; ICH within last 6/12; Severe menorrhagia; Known bleeding disorders
Weight (kg)		Use actual body weight (ABW)	<50kg or >120kg
Serum Creatinine (Cr)			dialysis
Calculated CrCl https://www.mdcalc.com/creatinine-clearance-cockcroft-gault-equation		DO NOT USE eGFR/IBW - USE Actual Body Weight Review medications that affect renal function if CrCl reduced	CrCl <15ml/min; consider CrCl <30ml/min
Concurrent medications		Review antiplatelets/NSAIDs Check for interactions	DAPT (dual antiplatelet therapy); Contraindications; Interacting medications :Refer to BNF interactions
BP (mmHg)		Address uncontrolled hypertension (systolic bp >160mmHg increases bleed risk)	
Alcohol consumption		Aim < 8 units per week	Known liver cirrhosis
Blood results		From within 3 months: U&Es, FBC, LFTs, Baseline clotting	Bilirubin >1.5 ULN; LFTs >2 x ULN; Plts <100; Abnormal clotting screen; Hb low with no identifiable cause
PMHx			TAVI in last 3/12; Active Cancer; Pregnant/planning a pregnancy; Breastfeeding

Which DOAC?

Following the completion of a national DOAC (direct oral anticoagulant) procurement exercise, NHS England & Improvement (NHSEI) has issued a DOAC commissioning guidance which recommends that clinicians use Edoxaban where appropriate as the DOAC of choice. Edoxaban is now the first line option in City and Hackney and Homerton hospital for patients who need to be initiated on a DOAC for prevention of stroke or systemic embolism associated with non-valvular atrial fibrillation (NVAF), subject to the criteria specified in the relevant NICE technology appraisal guidance.



DOAC dose summary table for non-valvular AF

	Dabigatran Big blue capsules	**Rivaroxaban** Small round tablets	**Apixaban** Small round/ oval tablets	**Edoxaban** Small round tablets
Standard dose	150mg BD	20mg OD (with food)	5mg BD	60mg OD
Reduced dose	110mg BD	15mg OD (with food)	2.5mg BD	30mg OD
Criteria for reduced dose	- Age ≥ 80 yrs - On verapamil - Consider for; • Reflux • Age 75-80 yrs • CrCl 30-50ml/min • "Bleed risk"	CrCl 15-49ml/min	≥ 2 of; - Age ≥ 80yrs - Wt ≤ 60kg - Cr ≥ 133µmol/L OR CrCl 15-29ml/min	≥ 1 of; - Wt ≤ 60kg - CrCl 15-50ml/min - On ciclosporin, dronedarone, erythromycin, ketoconazole
Contra-indicated	CrCl <30ml/min	CrCl <15ml/min		
Can be crushed?	No	Yes		
Can be put in a dosette box?	No	Yes		

Monitoring

After 1 month of DOAC initiation;

- Check for side effects – refer if present
- Check if seen for New Medicine Service at community pharmacy
- Adherence (including Rx refills)
- Thromboembolic events
- Bleeding events/risk factors
- Medication review (interactions + OTC meds)

Then MINIMUM YEARLY review (See table for requirement for more frequent renal monitoring);

- Age – check for dosage adjustment
- Weight – check for dosage adjustment
- FBC annually where in range – investigate any Hb drop
- LFTs annually where in range
- U&Es as per table
- Check calculated CrCl

Calc CrCl range (ml/min)	**How often to check renal function**
<15	DOAC contraindicated, refer to specialist
15-30	3 monthly
30-60	6 monthly
>60	12 monthly
Patients over the age of 75 years and / or frail. Routine surveillance every 6 months	

Counselling – see next page for checklist

Counselling checklist - https://www.cambridgeshireandpeterboroughccg.nhs.uk/easysiteweb/getresource.axd?assetid=20601&type=0&servicetype=1

Counselling points	Sign
Explanation of an anticoagulant (increases clotting time and reduces risk of clot formation) and explanation of Atrial Fibrillation	
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: lifelong	
To take with food (dabigatran and rivaroxaban). Not required for apixaban or edoxaban	
Missed doses: • Apixaban and dabigatran can be taken within 6 hours of missed dose, otherwise omit the missed dose • Edoxaban and rivaroxaban can be taken within 12 hours of missed dose, otherwise omit the missed dose	
Extra doses taken: obtain advice immediately from pharmacist/GP/NHS Direct (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 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's suitable for 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)	

Additional Information on switching from warfarin to a DOAC

Suggested process for safe switching from warfarin to a DOAC:

1. Check recent U&Es, LFTs, FBC and clotting screen (ideally within the last 3 months) and calculate creatinine clearance (CrCl) using actual body weight from last 12 months (unless recent weight loss/gain - *if patient <50kg or >120kg, refer to secondary care*).
2. Discuss options with your patient and/or carers (as appropriate) and, with consent, prescribe DOAC at appropriate dose – edoxaban preferred first-line.
3. **Remove warfarin from the repeat prescription after initiating DOAC.**
4. 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=%20e7e62356-8aa6-472a-aeb1-eb5b58315d49
5. 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.
6. Provide an up-to-date Anticoagulant Alert and DOAC counselling (see checklist).
7. Ensure appropriate on-going monitoring is in place using the clinical system recall function – frequency will depend on renal function, age and frailty.

When switching therapy, care should be taken to follow the recommendations in the relevant SmPC:

- Apixaban (Eliquis®): https://www.medicines.org.uk/emc/product/2878/smpc
- Dabigatran (Pradaxa®): https://www.medicines.org.uk/emc/product/4703/smpc
- Edoxaban (Lixiana®): https://www.medicines.org.uk/emc/product/6905/smpc
- Rivaroxaban (Xarelto®): https://www.medicines.org.uk/emc/product/2793/smpc

Additional Information on switching from another DOAC to edoxaban

Suggested process for each patient:

1. Check recent U&Es, LFTs and FBC (ideally within the last 3 months) and calculate creatinine clearance (CrCl) using actual body weight from last 12 months (unless recent weight loss/gain).
2. Discuss options with your patient and/or carers (as appropriate) and, with consent, prescribe edoxaban at appropriate dose.
3. **Remove current DOAC from repeat prescription after adding edoxaban.**
4. Advise patient to continue with existing DOAC whilst obtaining supplies - ideally the patient should switch to edoxaban after using up their existing supplies of the other DOAC.
5. Advise patient when to stop the alternative DOAC and when to start edoxaban:
    - **For patients on rivaroxaban:** continue as usual on the day before the switch; start edoxaban once daily when the next dose is due on the day of the switch. Continue once daily thereafter.
    - **For patients on apixaban or dabigatran:** continue with normal morning and evening dosing on the day before the switch; start edoxaban once daily when the next dose is due on the day of the switch. Continue once daily thereafter.

    Ensure the patient understands that the edoxaban should only be taken ONCE daily
6. Provide written instructions and involve family members / carers where possible . Particular care should be taken where patients are using medication compliance aids – ensure the community pharmacy is informed.
7. Provide an up-to-date Anticoagulant Alert card and DOAC counselling (see checklist).
8. Ensure appropriate on-going monitoring is in place using the clinical system recall function – frequency will depend on renal function, age and frailty.

In City & Hackney, we recommend that if practices/PCNs have the resources and expertise to review and switch patients from another DOAC to edoxaban safely then they may do so at their discretion. The ultimate decision to prescribe or make changes to prescriptions would lie with the clinician.

Appendix 1: CHA_2DS_2-VASc Score

www.mdcalc.com/cha2ds2-vasc-score-atrial-fibrillation-stroke-risk

(definitions from www.chadsvasc.org)

Risk Factor	Score
Congestive Heart Failure- The presence of signs and symptoms of either right or left ventricular failure or both, confirmed by non-invasive or invasive measurements demonstrating objective evidence of cardiac dysfunction. E.g. LVEF < 40%	1
Hypertension- A resting blood pressure >140mmHg systolic and/or >90mmHg diastolic on at least 2 occasions or current antihypertensive pharmacologic treatment	1
Age ≥ 75 yrs	2
Age 65-74 yrs	1
Diabetes mellitus- Fasting plasma glucose level ≥7.0 mmol/L (126 mg/dL) or treatment with oral hypoglycaemic agent and/or insulin	1
Stroke/TIA/thromboembolism	2
Vascular Disease- Prior myocardial infarction, angina pectoris, percutaneous coronary intervention or coronary artery bypass surgery. The presence of any the following: intermittent claudication, previous surgery or percutaneous intervention on the abdominal aorta or the lower extremity vessels, abdominal or thoracic surgery, arterial thrombosis	1
Sex female	1
TOTAL SCORE	

CHA_2DS_2-VASc Score	Adjusted Stroke Rate (% year)
0	0.2
1	0.6
2	2.2
3	3.2
4	4.8
5	7.2
6	9.7
≥ 7	≥ 11.2

Appendix 2: ORBIT Score

https://www.mdcalc.com/calc/10227/orbit-bleeding-risk-score-atrial-fibrillation

NICE AF guidelines (2021) now recommends to use the OBRIT bleeding risk score over HAS-BLED scoring system because evidence shows that it has a higher accuracy in predicting absolute bleeding risk. Please note a high ORBIT score is not a sole reason to withhold anticoagulation.

Risk Factor	Score
Males: Haemoglobin <13 g/dL or haematocrit <40% **Females:** Haemoglobin <12 g/dL or haematocrit <36%	2
Age > 75 yrs	1
Bleeding risk- Any history of GI bleeding, intracranial bleeding, or haemorrhagic stroke	2
GFR <60 mL/min/1.73 m^2	1
Labile INR- Unstable/high INR	1
Treatment with antiplatelet agents	1
TOTAL SCORE	

ORBIT Score	Risk group	Bleeds per 100 patient-years
0-2	Low	2.4
3	Medium	4.7
4-7	High	8.1