"Pointers" to DOAC treatment choices in non-valvular AF

No trials have directly compared different DOACs with each other, so it is difficult to determine which drug should be recommended as a first choice for most patients. The guidance below does not override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer, and informed by the summaries of product characteristics of any drugs.

ABSOLUTE CRITERIA FOR WARFARIN:
eGFR <15ml/min/1.73m^2, body weight <50kg & >120kg *or* BMI >40kg/m^2, any poorly compliant patient, mechanical heart valve, patients with HIV

Specific patient characteristics

Previous GI bleed /disorder	Consider agent/dose with fewer reported GI effects	apixaban
High risk of bleeding, e.g. HAS-BLED ≥ 3; very old	Consider agent/dose with the lowest incidence of bleeding (non specialists - consider seeking advice)	In order of acquisition cost – lowest first ▼edoxaban, dabigatran110mg*, apixaban
High risk of ischaemic stroke, low bleeding risk	Consider agent/dose with the best reduction of ischaemic stroke	dabigatran 150mg*
Previous stroke (secondary prevention)	Consider best investigated agent or greatest reduction of secondary stroke	In order of acquisition cost – lowest first ▼edoxaban, ▼rivaroxaban‡, apixaban
CAD, previous MI or high-risk for ACS/MI	Consider agent with a positive effect in ACS	▼rivaroxaban‡
Renal impairment See further information overleaf	Consider agent least dependent on renal function	In order of acquisition cost – lowest first ▼edoxaban 30mg (reduced dose), ▼rivaroxaban‡15mg, apixaban†
Patient preference	Consider once daily formulation	In order of acquisition cost – lowest first ▼edoxaban, ▼rivaroxaban‡

‡ take/administer **WITH FOOD**, † use endorsed by NICE CG182, * antidote available ; ACS=acute coronary syndrome; CAD=coronary artery disease; MI=myocardial infarction; DOAC= direct acting oral anticoagulant; ▼=drug is subject to additional monitoring. ***Note*: where more than one DOAC is an option, edoxaban is the preferred choice for ABUHB as it has a significantly lower acquisition cost due to an all Wales approved primary care rebate.**

FOR FULL PRESCRIBING INFORMATION CONSULT SmPC https://www.medicines.org.uk/emc/

Adapted from Savelieva I, Camm AJ. *Clin Cardiol* 2014;37:32–47 & Gonzalez-Quesada CJ, Giugliano RP. *Am J Cardiovasc Drugs* 2014;14:111–127. Date of preparation: March 2017 (Latest revision June 2019)

DOAC indications, doses, notable interactions & Traffic Light

DOAC (Brand with links to SmPC)	Dabigatran (Pradaxa®)		Rivaroxaban ▼ (Xarelto®)			Apixaban (Eliquis®)		Edoxaban ▼ (Lixiana®)	
Indication [NICE TA]	**AF [NICE TA 249]**	**DVT, PE [NICE TA 327]**	**AF [NICE TA 256]**	**DVT, PE [NICE TA 287]**	**ACS [NICE TA 335]**	**AF [NICE TA 275]**	**DVT, PE [NICE TA 341]**	**AF [NICE TA 355]**	**DVT, PE [NICE TA 354]**
TRAFFIC LIGHT:	GREEN	AMBER	GREEN	AMBER	AMBER	GREEN	AMBER	GREEN	AMBER
DOSES:	Age < 80 yrs - **150mg twice daily** **Age ≥ 80 yrs** or taking **verapamil** - **110mg twice daily** Following individual assessment of the individual risk of thromboembolism and bleeding consider **110mg twice daily if:** - bleeding risk is high - age 75-80 yrs - patients with gastroesophageal reflux, oesophagitis or gastritis - CrCL 30-50ml/min	Following parenteral anticoagulant for at least 5 days - **150mg twice daily** Duration of treatment individualised after careful assessment of the treatment benefit against the risk of bleeding	**20mg once daily** **15mg once daily** when CrCL is 15-49 ml/min	15mg twice a day for 21/7 then 20mg daily (min. 3/12) 10mg daily for extended prevention of recurrent DVT & PE (after ≥6 months therapy for DVT/PE) CrCL 15-49 ml/min - 15mg twice a day for 21/7 then 20mg daily (or 15mg daily if risk of bleeding > risk of recurrent DVT & PE)	2.5mg twice daily with: -aspirin alone **Or** -aspirin plus clopidogrel or ticlopidine Use with caution if >75yrs or if <60kg Review regularly. Extension of treatment beyond 12 months should be done on an individual basis	**5mg twice daily** CrCL 15-29ml/min - 2.5mg twice daily Patients with two or more of the following give **2.5mg twice daily:** -age ≥80 yrs -body weight ≤60kg -serum Cr ≥133 micromole/l **Or** All patients with severe renal impairment (CrCL 15–29 ml/min)	**Treatment** dose DVT/PE - 10mg twice daily for the first 7 days followed by 5mg twice daily **Prevention** DVT/PE following 6/12 treatment dose – 2.5mg twice daily The duration of treatment should be individualised after careful assessment of the treatment benefit against the risk of bleeding	60mg once daily Patients with one or more of the following give **30mg daily:** - CrCL 15-50ml/min -body weight <60kg -concurrent P-gp inhibitors: ciclosporin, dronedarone or erythromycin	Following parenteral anticoagulant for at least 5 days - 60mg once daily Duration of treatment individualised after careful assessment of the treatment benefit against the risk of bleeding
RENAL IMPAIRMENT	Patients must have baseline renal function and recent weight before initiating NOAC. **Renal function can decline while on treatment. Monitor annually with normal renal function (6 monthly if >75-80 yrs [especially if dabigatran or edoxaban], or frail), otherwise a good guide is the eGFR divided by 10 in months and a low threshold to check renal function during inter-current illness/dehydration. Patient's weight should be rechecked at each renal monitoring visit.** Although eGFR and CrCL are NOT considered interchangeable (for most drugs and for most patients [>18 years] of average build and height, eGFR provides some guidance) **if a patient's eGFR figure is close to the threshold for a dose reduction use the 'Cockcroft-Gault' formula to confirm CrCL** (dabigatran & edoxaban SmPCs advise using Cockcroft-Gault for dosing/monitoring **Cockcroft-Gault formula**: **CrCL = (140-Age in yrs) x Weight* (kg) x Constant / Serum creatinine** (use: https://www.mdcalc.com/) *Constant = 1.23 (Men); 1.04 (Women). Serum creatinine (in micromoles/litre)]* *In the RE-LY, ROCKET-AF and ARISTOTLE trials for dabigatran, rivaroxaban and apixaban, **total (actual) body weight** (rather than Ideal or Adjusted Body Weight) was used for CrCL calculations in the Cockcroft-Gault equation. **Use warfarin for those with a body weight <50kg & >120kg**								
Some notable DRUG INTERACTIONS: CONSULT SMPC FOR FULL DETAILS	Avoid concomitant use of **rifampicin, phenytoin, carbamazepine, phenobarbital or St. John's Wort** - the anticoagulation effect of all 4 DOACs **reduced** Avoid concomitant use of **ketoconazole, itraconazole, voriconazole, posaconazole**, HIV protease inhibitors (e.g. **ritonavir**) - the anticoagulation effect of all 4 DOACs **increased** Close clinical surveillance (looking for signs of bleeding or anaemia) is recommended in patients treated concomitantly with **NSAIDs** (including acetylsalicylic acid), **anti-platelets** or **SSRIs**, and **SNRIs**, or any other drugs that can typically increase the risk of bleeding								
	Concomitant treatment with **ciclosporin** and **dronedarone** contraindicated **SSRIs** and **SNRIs** increased the risk of bleeding in RE-LY in all treatment groups Use **110mg twice daily** in those on concomitant **verapamil**		Avoid concomitant use with **dronedarone**			Diltiazem, naproxen, amiodarone, verapamil or quinidine may increase apixaban plasma concentration		With concomitant use of **ciclosporin, dronedarone** or **erythromycin** use edoxaban 30mg once daily	

Note: The Traffic Light designation of DOACs used for primary prevention of venous thromboembolic events (VTE) in adult patients who have **undergone elective hip or knee replacement** surgery is **RED** - The full supply should be made by the responsible surgeon and this use **is not covered by this guidance.**