Guidance for anticoagulation treatment choices in non-valvular atrial fibrillation (AF)

NHS
Kernow
Clinical Commissioning Group

Absolute criteria for warfarin: CRCL <15/min/1.73m2 (but consider warfarin in those with CKD 4 or above ie CRCL< 30ml/min1.73m2), do not use eGFR for dosing guidance as per SPC), body weight <50kg and >120kg or extremes of BMI, any poorly compliant patient, mechanical heart valve, people with moderate to severe aortic stenosis or of rheumatic origin and people with HIV.

Specific patient characteristics for DOAC consideration and warfarin considered inappropriate:

High risk of GI upset/ disorder	Consider agent / dose with fewer reported GI effects	Apixaban 5mg BD Edoxaban 30mg OD or Dabigatran* 110mg BD for those with reduced renal function/need for low dose as per SPC
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, Dabigatran 110mg *, 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 of ACS/MI	Consider agent with a positive effect in ACS	Rivaroxaban ±
Need for concomitant antiplatelet (ACS/stents)	Data from PIONEER and RE-DUAL studies	Dabigatran* or Rivaroxaban± (SAPT)
Renal impairment (see further information on AF in CKD factsheet)**	Consider agent least dependent on renal function	In order of acquisition cost - lowest first Edoxaban 30mg, rivaroxaban 15mg, apixaban¥ (also depends on weight and age)
Patient preference	Consider once daily formulation	In order of acquisition cost- lowest first Edoxaban, rivaroxaban±
Effective reversal agent / need for urgent thrombolysis	Need for idarucizumab (hospital only)	Dabigatran*

± take/administer with food; ¥ use endorsed by NICE CG182; * antidote available; ACS =acute coronary syndrome; CAD =coronary artery disease; MI = myocardial infarction; SAPT =single antiplatelet therapy. Where more than one DOAC is an option, edoxaban (with the lowest acquisition cost) should be considered at the time of writing.
** NB use of DOAC in CRCL <30ml/min with caution as some were excluded in trials and contraindicated for dabigatran

Adapted from NHS Wales, Guildford and Waverley CCG and Surrey Health CCG AF in the Prescribing clinical Network, NICE CG180 and NICE CG182, 2016 ESC guidelines for the management of AF, 2018 EHRA practical guide on the use of non-vitamin K oral anticoagulants in patients with AF

NOAC indications, doses, notable interactions and traffic light

NOAC (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 five 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 and 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 and 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 seven 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 five 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 (six 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: 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 and >120kg			
Some notable drug intereactions. Consult SMPC for full details.	Avoid concomitant use of rifampicin, phenytoin, carbamazepine, phenobarbital or St. John's Wort - the anticoagulation effect of all four NOACs reduced. Avoid concomitant use of ketoconazole, itraconazole, voriconazole, posaconazole, HIV protease inhibitors (e.g. ritonavir) - the anticoagulation effect of all four NOACs increased. Close clinical surveillance (looking for signs of bleeding or anaemia) is recommended in patients treated concomitantly with NSAIDs (including acetylsalicylic acid), anti-platelets and 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 NOACs 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.

Adapted from Savelieva I, Camm AJ. Clin Cardiol 2014;37:32–47 & Gonzalez-Quesada CJ, Giugliano RP. Am J Cardiovasc Drugs 2014;14:111