Hertfordshire and West Essex Integrated Care System

NHS Hertfordshire and West Essex Integrated Care Board

Guidelines for oral anticoagulation of patients with non-valvular atrial fibrillation (AF) to prevent stroke in adults.

Contents

1. Atrial fibrillation anticoagulant; overview & checklist

1.1. Risk assessments

CHA_2DS_2Vasc Score		**ORBIT Score**		**See page 3**
Annual Stroke Risk		**Annual Bleed Risk**		
Modifiable Risk Factors				**See page 4**
Contra-indications to anticoagulation				**See page 4**

1.2. Baseline clinical screening checklist

	U&Es (Creatinine)	CrCl using Cockcroft & Gault formula	Weight* (kg)	FBC	LFTs	Baseline Clotting	BP
Baseline (All patients)							

**Recent weight, ideally at time of clinical screening*

1.3. Choice of anticoagulant and further information

Direct oral anticoagulant DOAC or warfarin (or alternative vitamin K antagonist (VKA)).		**See page 5-6**
If DOAC is the preferred choice; generic apixaban and rivaroxaban are best value twice a day and once a day treatment choice. In the absence of specific patient characteristics determining choice, least expensive appropriate DOAC to be used.		
****Interactions with patient's current medicines**		**Consult product literature for interacting drugs – check SPCs for full list.** **further useful information on common interactions with OAK therapy can be found on the following:** • **Triple therapy (dual antiplatelet therapy plus OAK) see page 6; discuss with specialist** • **Managing interactions with DOACs (SPS)** • **The European Society of Cardiology 2024 ESC Guidelines for the management of atrial fibrillation – figure 9 '*common drug interactions with oral anticoagulants*' (link)**
****DOAC Dose**		**See page 7** **Creatinine Clearance (CrCl) using Cockcroft & Gault formula see page 8**
****Patient Counselling**		**See appendix 1:** *Example DOAC counselling checklist*
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1.4. Ongoing Monitoring

DOAC	**U&Es (Creatinine, CrCl Using Cockcroft & Gault formula, Weight (kg), FBC, LFTs, BP**	**See page 9**
Warfarin/VKA		**See page 10**

2. Assessment of stroke and bleeding risks for patients with non-valvular AF

Online calculators are available on GP clinical systems

- CHA2DS2-VASc scoring system for risk of stroke
  Scoring Calculator: https://www.mdcalc.com/cha2ds2-vasc-score-atrial-fibrillation-stroke-risk
- ORBIT scoring system for risk of bleed (***recommended bleeding risk tool by NICE guidance 196: Atrial fibrillation: diagnosis and management***)
  Scoring Calculator: https://www.mdcalc.com/orbit-bleeding-risk-score-atrial-fibrillation

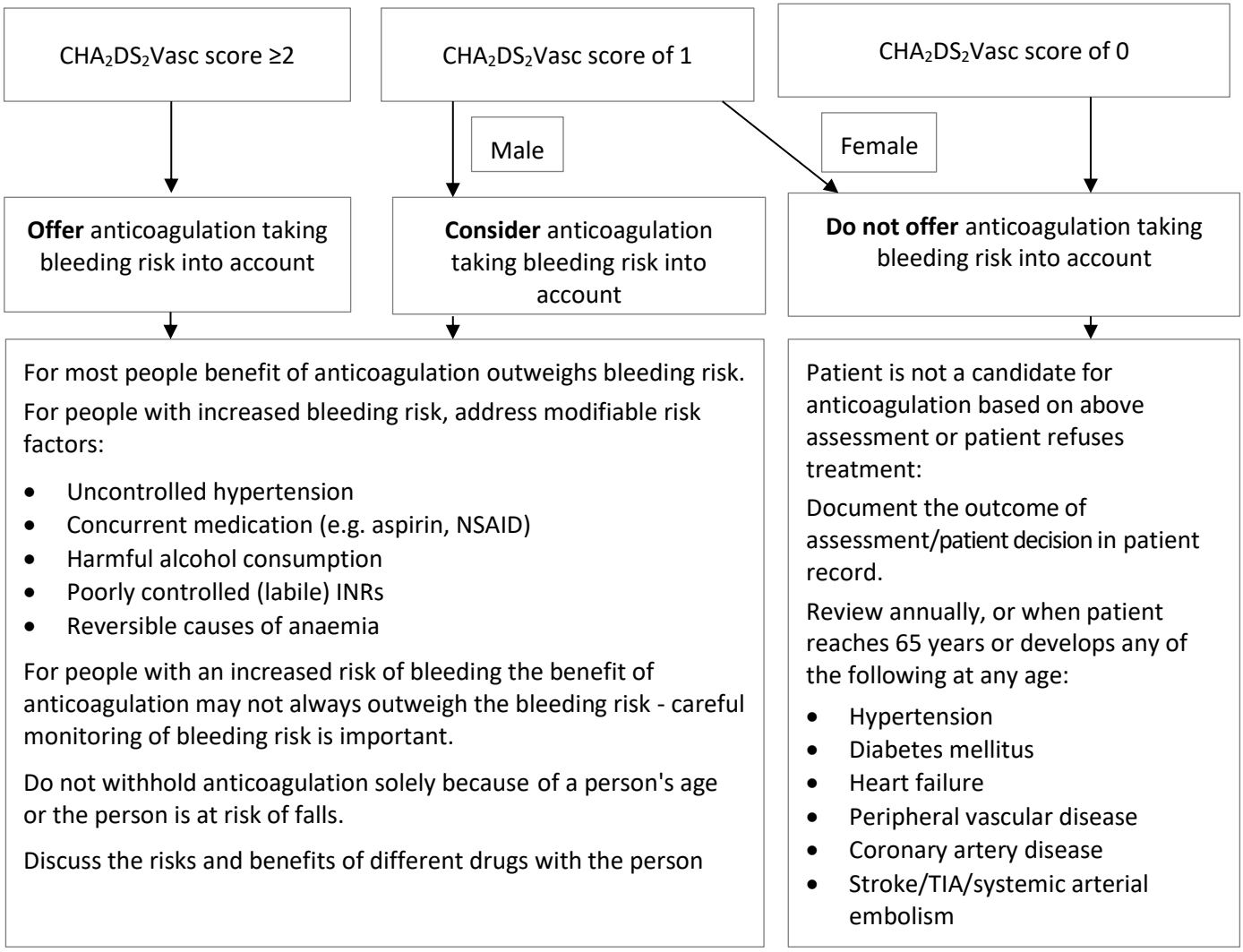
CHA_2DS_2Vasc Scoring System for AF Stroke Risk[1,2,3]		ORBIT scoring for Bleeding Risk[4]	
Risk Factor	**Score**	**Risk Factor**	**Score**
Congestive heart failure/LV dysfunction	1	Males with haemoglobin <130 g/L or haematocrit <40%.	2
Hypertension	1	Females with haemoglobin <120 g/L or haematocrit <36%.	
Age ≥ 75	2	People with a history of bleeding (gastrointestinal or intracranial bleeding, or haemorrhagic stroke)	2
Diabetes mellitus	1	Aged over 74 years	1
Stroke/TIA/systemic arterial embolism	2	estimated glomerular filtration rate (eGFR) of less than 60 mL/min/1.73m^2	1
Vas**c**ular disease (previous MI, peripheral arterial disease, aortic plaque)	1	Treatment with antiplatelets	1
Age 65 -74	1		
Sex (male 0, female 1)	F 1		
Total score *(maximum score 9)*		**Total score** *(maximum score7)*	

Interpreting CHA_2DS_2Vasc and ORBIT Score

CHA_2DS_2 Vasc	Events per 100 patients/year		ORBIT Score**	Bleeds per 100 patient-years
	Stroke/TIA/peripheral emboli	Ischaemic stroke		
0	0.3	0.2	0	1.7
1	1.0	0.6	1	2.3
2	3.3	2.5	2	2.9
3	5.3	3.7	3	4.7
4	7.8	5.5	4	6.8
5	11.7	8.4	5	9.0
6	15.9	11.4	6	12.3
7	18.4	13.1	7	14.9

**score 0-2: low risk, 3 medium risk, 4-7: high risk

3. Prescriber decision support for anticoagulating patients with non-valvular AF



(Flow diagram adapted from AF (non-valvular): prescriber decision support for anticoagulation, Nottinghamshire Area Prescribing Committee; flow diagram updated March 2022 in line recommendations form NICE CG196)

Contra-indications to anticoagulation[3,5-11]

The following list of contraindications are taken from individual Summary of Product Characteristics (SPC's)[5-8], MHRA safety updates 2009[9] and 2013[10], NICE CKS[11] and European Society of Cardiology guidelines for the management of atrial fibrillation 2020[3]. The list below is not exhaustive; see individual SPCs for additional contraindications for individual anticoagulants (https://www.medicines.org.uk/emc)

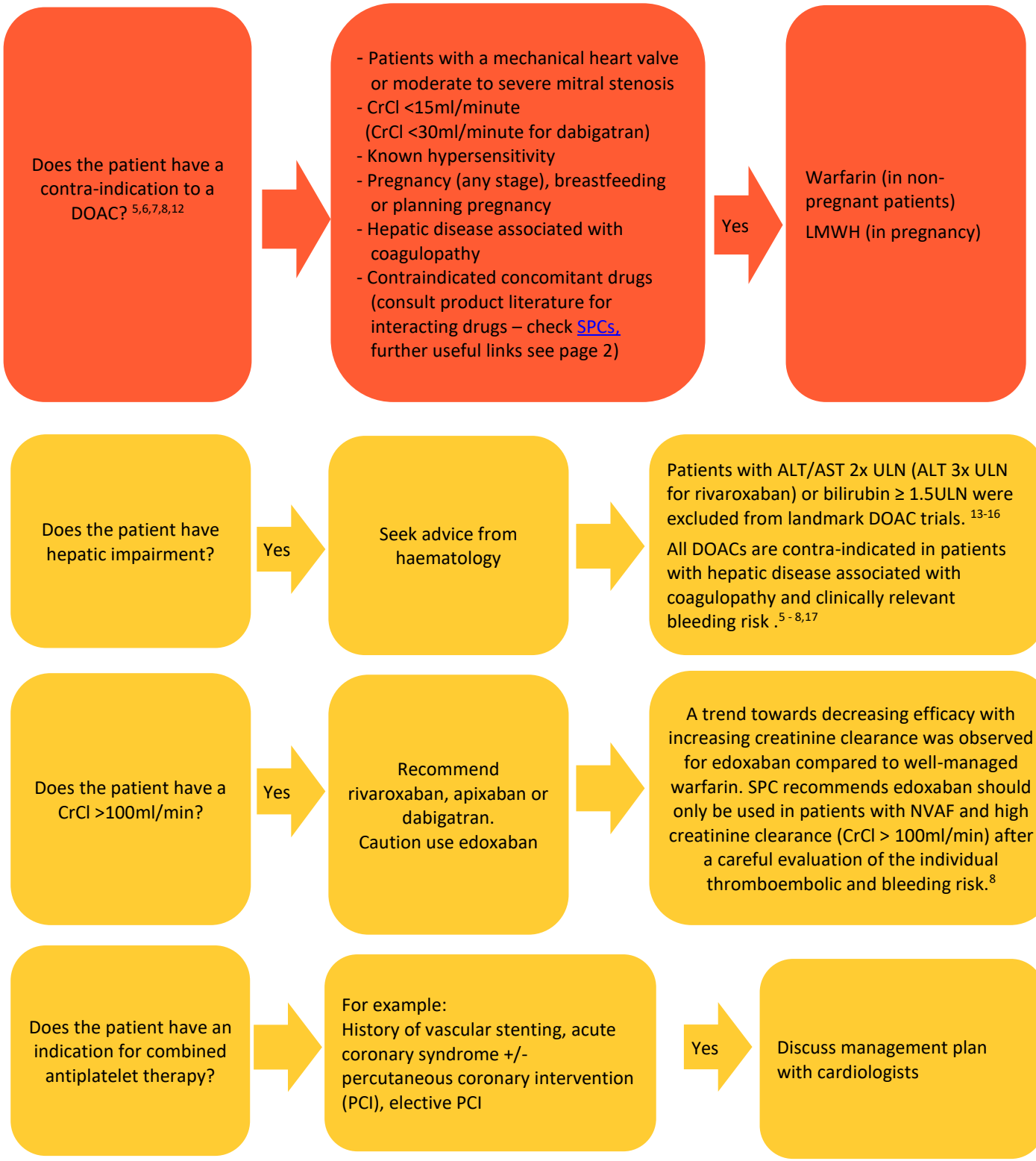
Discuss the clinical management plan with a specialist if there is a clear contraindication to anticoagulation treatment; re-assess risk factors regularly (some contra-indications may be temporary) and/or consider other non-drug treatment strategies (e.g. left atrial appendage occlusion device).[12]

- Clinically significant bleeding
- Recent intracranial haemorrhage
- A significant risk of major bleeding such as:
    - Current or recent upper gastrointestinal ulceration
    - Presence of malignant neoplasm at high risk of bleeding
    - Known or suspected oesophageal varices
    - Recent brain, head or spinal injury/surgery or ophthalmic surgery
    - Arteriovenous malformation, vascular aneurysm or major intraspinal or intracerebral vascular abnormalities
    - Within 72 hours of major surgery
    - Thrombocytopenia platelets $<50 \times 10^9$/L
- Concomitant treatment with any other anticoagulant

4. Choice of oral anticoagulant based on patient characteristics

NICE CG 196 places direct-acting oral anticoagulants as the preferred anticoagulant for treatment of atrial fibrillation, unless contraindicated, not tolerated or not suitable. When direct-acting oral anticoagulants are contraindicated, not tolerated or not suitable, a vitamin K antagonist may be offered. Those already taking a vitamin K antagonist and are stable may continue with their current medication and discuss the option of switching treatment at their next routine appointment, taking into account the person's time in therapeutic range[1].

NB: Patients should already have been screened for an absolute contraindication to oral anticoagulation as per guidance on page 4.



Does the patient weigh more than 120kg or have a BMI greater than 40kg/m^2?

Yes

DOAC*/warfarin
Discuss with patient

Discuss with specialist if required – this may be especially important for scheduled procedures e.g. cardioversion, ablation

Weight >150kg /BMI>50kg/m^2; recommend warfarin

*Limited/less robust data on DOACs in extreme obesity; underrepresented in main DOAC RCT publications.
More data is emerging (from post hoc analyses and meta-analyses) that DOACs have comparable efficacy and safety compared to warfarin. [17,18,19] Society guidance positions; no consensus statement issued by ESC[17]; ACC/AHA considers in obesity BMI≥40kg/m^2 DOACs are reasonable to choose over warfarin for stroke risk reduction[18] Feedback from local clinicians noted in clinical practice, guidance from ISTH VTE is extrapolated to atrial fibrillation recommending standard dosing of apixaban and rivaroxaban. [20]

SPCs (DOACs) do not limit use in obesity (no cautions or contra-indications stated for this patient group). Dose as per recommendations in respective SPCs.[5-8]

Shared decision making is recommended after an informed discussion noting limitations of available evidence for DOACs in morbidly obese patients.

Patient history of non-compliance or are they likely to miss doses?

Yes

Consider warfarin

The protective effect of DOACs on the risk of stroke may fade 12 - 24 hours after a dose is taken.[5,6,7,8]
Warfarin allows monitoring of effectiveness if non-compliance is anticipated.

Has the patient been diagnosed with antiphospholipid syndrome?

Yes

Warfarin or refer to haematology

DOACs are not recommended in patients with antiphospholipid syndrome, particularly high-risk patients (those who test positive for all 3 antiphospholipid tests - lupus anticoagulant, anti-cardiolipin antibodies, and anti-beta 2 glycoprotein I antibodies), as they could be associated with increased rates of recurrent thrombotic events compared with therapy with a vitamin K antagonist.[21]

Direct-acting oral anticoagulants are the preferred anticoagulant for treatment of atrial fibrillation, unless contraindicated, not tolerated or not suitable.[1]

Yes

Initiate DOAC; if there are no specific clinical consideration or patient specific characteristics determining a DOAC choice, use the best value DOAC:

- **Generic prescribing apixaban for twice daily dosing regimen**
- **Generic prescribing rivaroxaban for once daily dosing regimen**[22]
- **In the absence of specific patient characteristics determining choice, least expensive appropriate DOAC to be used**

5. DOAC dosing for stroke risk reduction in non-valvular AF

- NB: The dose guidance below is specific to the use of DOAC therapy for stroke risk reduction in AF. Dosing recommendations for deep vein thrombosis, pulmonary embolism, acute coronary syndrome or post-hip/knee replacement can be found in the individual Summary of Product Characteristics via https://www.medicines.org.uk/emc
- Always check the latest Summary of Product Characteristics https://www.medicines.org.uk/emc for dosage adjustments (e.g. in liver impairment) and drug interactions before prescribing.
- See **page 10** for calculating **creatinine clearance using the Cockcroft-Gault equation for DOAC dose calculation**
- In general, as there is insufficent evidence for efficacy at lower doses for some agents, doses of DOACs should not be reduced unless a dose reduction is clinically indicated as outlined in the table below.

Dabigatran[5]	**Rivaroxaban**[6] **FIRST LINE ONCE DAILY DOAC OF CHOICE**	**Apixaban**[7] **FIRST LINE TWICE DAILY DOAC OF CHOICE**	**Edoxaban**[8]
Standard dose: **150mg TWICE daily**	Standard dose: **20mg ONCE daily**	Standard dose: **5 mg TWICE daily**	Standard dose: **60mg ONCE daily**
Reduce dose to: **110mg TWICE daily** If 1 or more of the following risk factors: • age ≥ 80yrs • taking verapamil Or consider reducing based on an individual assessment of the thromboembolic and bleeding risk if the following: • age 75-80yrs • CrCl 30-50ml/min • patients with gastritis, oesophagitis or gastroesophageal reflux • patients at increased risk of bleeding	Reduce dose to**:** **15mg ONCE daily** If the following risk factor: • CrCl 15 - 49 ml/min	Reduce dose to: **2.5 mg TWICE daily** If 2 or more of the following risk factors: • age ≥ 80 yrs • weight ≤ 60kg • serum creatinine ≥ 133 micromol/L Or • CrCl 15 - 29ml/min	Reduce dose to: **30mg ONCE daily** If 1 or more of the following risk factors: • CrCl 15 - 50ml/min • weight ≤ 60kg • concomitant use of P-gp inhibitors: o ciclosporin o dronedarone o erythromycin o ketoconazole
Extremes of body weight: No dose adjustment required. SPC notes close clinical surveillance if weight<50kg (limited data; plasma levels may be increased)	**Extremes of body weight:** No dose adjustment required	**Extremes of body weight:** No dose adjustment required. Use licensed dose. Low body weight in combination with other risk factor, see above – dose reduce.	**Extremes of body weight:** Dose reduce to 30mg once daily if weight ≤60kg

Calculating renal function – Cockroft and Gault formula

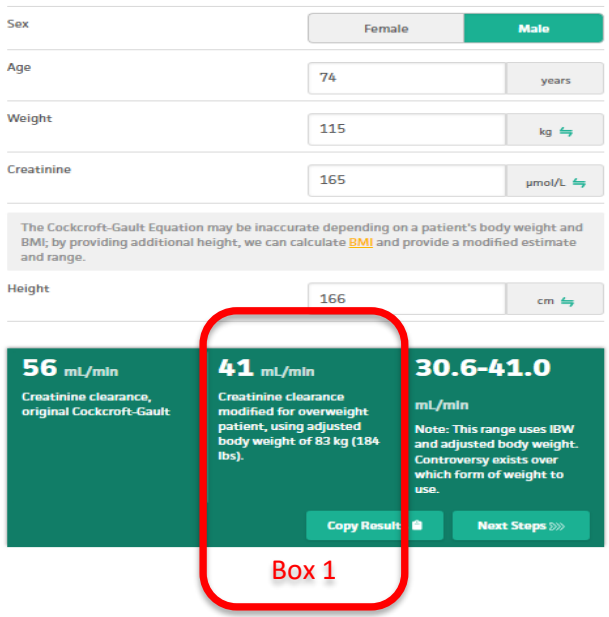
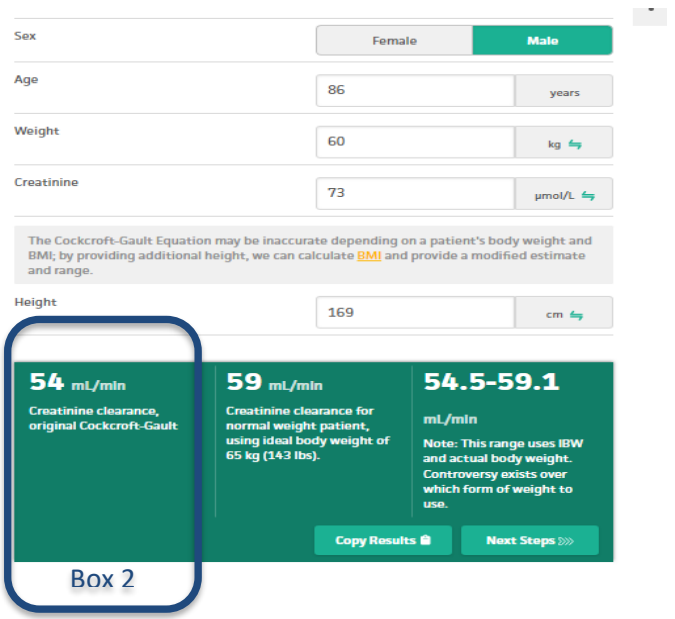
Use the Cockcroft-Gault equation for calculating creatinine clearance (CrCl) when prescribing DOAC therapy.[23] eGFR must not be used as data suggest it may lead to inappropriate dosing in up to 50% of patients.[24]

Cockcroft-Gault Equation for calculating Creatinine Clearance (CrCl)

$$\text{CrCl (ml/minute)} = \frac{(140\text{-age}) \times \text{weight}^*}{\text{Serum Creatinine (micromol/L)}} \quad \text{x 1.23 (male) or x 1.04 (female)}$$

*using actual body weight, unless the patient is obese (120kg or BMI ≥ 40 kg/m2/); then use adjusted body weight
(Adjusted body weight = Ideal body weight + 0.4 x (actual body weight – ideal body weight))

The MD+CALC on line calculator can be used to calculate patients CrCl https://www.mdcalc.com/creatinine-clearance-cockcroft-gault-equation

Example 1 using adjusted body weight (box 1) for overweight patient BMI>40	Example 2 using actual body weight (box 2)
	

***Weight:** The clinical trials of DOACs used actual body weight when estimating CrCl for patients. However the number of patients with obesity within the DOAC trials were small, in addition it is recognised that there are inaccuracies in estimating CrCl using the Cockcroft-Gault equation at extremes of body weight. Therefore for morbidly obese (BMI ≥ 40 kg/m^2/120kg) patients estimate the CrCl range using adjusted body weight (ABW) - local recommendation in line with PCCS/UKCPA/PCPA[28] . This applies an adjustment of 40% of the patient's excess weight over their ideal body weight (IBW). IBW for men = 50 kg + 2.3 kg for each inch over 5 feet and for women IBW = 45.5 kg + 2.3 kg for each inch over 5 feet

6. DOAC monitoring and follow-up

All patients on long-term anticoagulants require a general review at least once a year or more frequently if clinically relevant events occur affecting anticoagulation or bleeding risk. [1]
SPS/NICE CKS further recommend a DOAC review appointment after 1month of initiation, then annually thereafter or more frequent depending on patient factors, such as renal function, age, and comorbidities.[11,26]
Annually - Blood sampling (FBC, LFTs, U&Es including creatinine) or as recommended in the table below.

Each DOAC review appointment:

- Assess adherence to treatment.
- Look for signs of bleeding or anaemia.
- Ask about other adverse effects of DOAC. (See SPC for adverse effects)
- Assess for features of thromboembolic events, such as symptoms of stroke, or breathlessness (which may suggest a pulmonary embolism).
- Check on the use of other medications, including over-the-counter products, to identify possible drug interactions with DOAC.
- Assess and minimize modifiable risk factors for bleeding, such as uncontrolled hypertension, medication predisposing for bleeding (such as aspirin), and excessive alcohol intake.
- Give appropriate information and advice on DOAC treatment.

Blood sampling and weight (see table below on recommended monitoring frequency):

Patient group	U&Es	CrCl	FBC	LFTs	BP	Clotting screen	Weight
Baseline (All patients)	Yes	Yes	Yes	Yes	Yes	Yes	Yes
CrCl > 60ml/min	Annually	Annually	Annually	Annually	Annually	NA	Minimum annually – more recent weight may be required if recent weight gain/loss
Age ≥ 75 years, frail	4 monthly	4 monthly	4 monthly	4 monthly	Annually		
***CrCl 30-60ml/min**	Minimum 6 monthly	Minimum 6 monthly	Minimum 6 monthly	Minimum 6 monthly	Annually		
** PCCS/UKCPA/PCPA[25] recommend routine surveillance 6 monthly in CrCl 30-60mls/min/min. NICE CKS[11] and SPS[26] recommend that if CrCl < 60 mL/min, the frequency of monitoring (in months) can be guided by the CrCl divided by 10. For example, every 3 months if CrCl is 30 mL/minute.*							
****CrCl <30ml/min or an expected decline in renal function**	Minimum 3 monthly	Minimum 3 monthly	Minimum 3 monthly	Minimum 3 monthly	Annually		
*** PCCS/UKCPA/PCPA[25] routine surveillance 3 monthly in CrCl 15-30mls/min. NICE CKS[11] and SPS[26] recommend that if CrCl < 60 mL/min, the frequency of monitoring (in months) can be guided by the CrCl divided by 10. For example, every 3 months if CrCl is 30 mL/minute.*							
Intercurrent condition that may impact renal or liver function	If needed	If needed	If needed	If needed	If needed		

Assess of if chosen OAC/DOAC remains the best choice and chosen dose is correct.

7. Warfarin monitoring and follow-up

All patients on long term anticoagulants require a general review at least once a year or more frequently if clinically relevant events occur affecting anticoagulation or bleeding risk: [1]

- **Assessment of Stroke and Bleeding Risk**
    - Recalculate CHA_2DS_2-VASc and bleeding risk score to confirm if risk/benefit remains unchanged
    - Enquire about the presence of bleeding (Nuisance or Impacting on QOL)
    - Identify and minimise any modifiable risk factors
    - Confirm anticoagulation is still appropriate
- **Where suitable, discuss option to switch to a direct-acting oral anticoagulant**
- **Assessing anticoagulation control with warfarin**

  Calculate the person's time in therapeutic range (TTR) at each visit. When calculating TTR:
    - Use a validated measurement method
    - Exclude measurements taken during the first 6 weeks of treatment
    - Calculate TTR over a maintenance period of at least 6 months
- **Reassess anticoagulation for a person with poor anticoagulation control shown by any of the following:**
    - INR values higher than 5 OR 1 INR value higher than 8 within the past 6 months
    - INR values less than 1.5 within the past 6 months
    - TTR less than 65%
- **When reassessing, take into account and if possible, address the factors that may contribute to poor control:**
    - Patient education
    - Cognitive function
    - Adherence to prescribed therapy
    - Illness
    - Interacting drugs
    - Lifestyle factors including diet and alcohol
    - Inconvenient/inappropriate monitoring arrangements – confirm suitability and consider self-monitoring and self-management arrangements, consider domiciliary monitoring arrangements for those patients with reduced mobility.
- **For all patients deemed to have failed on warfarin therapy, establish relevant anticoagulant treatment history. Confirm evidence to support proposed reason for treatment failure, for example:**
    - Failed monitoring arrangements – did the patient attend an anticoagulant monitoring service?
    - Labile INR – did the patient achieve a therapeutic INR?
    - Bleeding complications – was the bleed major/ minor? Confirm INR at time of bleed.
    - Drug interactions – any change to concurrent therapy should be considered.
    - Serious ADR – was this documented in patient's records?
    - Severe alopecia – was the patient offered alternative VKA agents?
- **If poor INR control cannot be improved, evaluate the risks and benefits of alternative stroke prevention strategies and discuss this with the patient.**

8. Communication across secondary/primary care interface - Information to be transferred to primary care

Letters to GPs from secondary care, when anticoagulation has been initiated in secondary care, to include all of the following information:

- Baseline assessment results: CHA_2DS_2-VASc score, ORBIT score, renal function as CrCl, haemoglobin, platelets.
- Discussion with patient/carer:
    - Likelihood of stroke in the individual patient in next year
    - Likelihood of benefit with OAC (NB: It is important that patients/carer understand that there is never 100% certainty that treated patients will not have a stroke).
    - Likelihood of major bleeding in next year
    - Implications of OAC on major bleeding
    - Choice of OAC. (See clinical decision aid)
- Information to be given to patient:
    - Anticoagulant alert card
    - Information for monitoring bleeds
    - Patient leaflet on oral anticoagulants

Appendix 1: Example DOAC patient counselling checklist

The following should be discussed with all patients started on oral anticoagulation and should be documented in the patient record.

Patient information given	√
Explain purpose.	
Dose and frequency.	
Timing of doses. Ensure that rivaroxaban is taken with food.	
Duration of treatment.	
Importance of compliance and what to do if doses are missed – see patient information leaflet	
Explain serious side effects • Bleeding - Seek urgent medical attention if patient develops severe bleeding, e.g. blood in faeces, vomit or sputum, vaginal bleeding. • Advise to seek urgent medical attention if they fall or injure themselves during treatment, especially if they hit their head, due to the increased risk of bleeding. • Unusual headaches.	
Need to inform medical staff that they are taking DOAC if prescribed new medications or surgery /or if invasive procedures (including dental extractions) being planned. Bleeding risk if DOAC started immediately post op.	
Possible interactions with other drugs including herbal remedies - advise patient to read patient information leaflet and discuss with pharmacist or doctor before taking any over the counter remedies.	
Avoid aspirin or NSAIDs (unless clinically indicated)	
Advise patient to seek advice if planning to become pregnant or breastfeed	
Referral to Community Pharmacy New Medicines Service (NMS) – suitable for patients prescribed anticoagulants for the first time	
Monitoring and review: review of treatment and blood tests at least once a year but may be more frequent for some patients **(see monitoring requirements)**	
Alert card and patient information given	

Appendix 2: Switching between oral anticoagulants for non-valvular atrial fibrillation

Consult the Summary of Product Characteristics for each individual anticoagulant for further information.[5-8,11]

Switching from	Switching to Warfarin	Dabigatran	Edoxaban	Rivaroxaban	Apixaban	Low Molecular Weight heparin (LMWH)
Warfarin		Discontinue warfarin and start dabigatran: When INR is ≤ 2	Discontinue warfarin and start edoxaban: When INR is ≤ 2.5	Discontinue warfarin and start rivaroxaban: When INR is ≤ 3	Discontinue warfarin and start apixaban: When INR is ≤ 2	Initiate prophylactic or treatment dose LMWH once INR below 2
	INR values may be falsely elevated after the intake of DOACs					
Apixaban	Commence warfarin in combination with apixaban. Apixaban should be continued for 2 days, after which point INR should be measured prior to each dose of apixaban. Apixaban should be discontinued when INR is ≥ 2.0.	Discontinue apixaban and commence dabigatran at the time that the next dose of apixaban would be due.	Discontinue apixaban and commence edoxaban at the time that the next dose of apixaban would be due.	Discontinue apixaban and commence rivaroxaban at the time that the next dose of apixaban would be due.		Discontinue apixaban and commence LMWH at the time that the next dose of apixaban would be due.
Dabigatran	Conversion protocol depends on renal function: For CrCl ≥ 50ml/minute, commence warfarin 3 days prior to discontinuing dabigatran. For CrCl 30-50ml/minute, commence warfarin 2 days prior to discontinuing dabigatran. NB: dabigatran can increase INR. INR measurements should be interpreted cautiously until dabigatran has been stopped for 2 days.		Discontinue dabigatran and commence edoxaban at the time that the next dose of dabigatran would be due.	Discontinue dabigatran and commence rivaroxaban at the time that the next dose of dabigatran would be due.	Discontinue dabigatran and commence apixaban at the time that the next dose of dabigatran would be due.	Discontinue dabigatran and commence LMWH 12-hours after the last dose of dabigatran was administered.
Edoxaban	Patients on 60 mg dose of edoxaban; administer edoxaban at a dose of 30 mg once daily together with warfarin. Patients 30 mg dose of edoxaban; administer edoxaban at a dose of 15 mg once daily together with warfarin. Measure the INR just prior to the daily dose of edoxaban, continue edoxaban until the INR is ≥ 2.0.	Discontinue edoxaban and commence dabigatran at the time that the next dose of edoxaban would be due.		Discontinue edoxaban and commence rivaroxaban at the time that the next dose of edoxaban would be due.	Discontinue edoxaban and commence apixaban at the time that the next dose of edoxaban would be due.	Discontinue edoxban and commence LMWH at the time that the next dose of edoxaban would be due.
Rivaroxaban	Commence warfarin in combination with rivaroxaban. Rivaroxaban should be discontinued when INR is in therapeutic range. Measure INR prior to each dose of rivaroxaban being administered.	Discontinue rivaroxaban and commence dabigatran at the time that the next dose of rivaroxaban would be due.	Discontinue rivaroxaban and commence edoxaban at the time that the next dose of rivaroxaban would be due.		Discontinue rivaroxaban and commence apixaban at the time that the next dose of rivaroxaban would be due.	Discontinue rivaroxaban and commence LMWH at the time that the next dose of rivaroxaban would be due.

Switching from	Switching to Warfarin	Dabigatran	Edoxaban	Rivaroxaban	Apixaban	Low Molecular Weight heparin (LMWH)
Low Molecular Weight Heparin (LMWH)	Commence warfarin in combination with LMWH, and monitor INR. Discontinue LMWH once INR in therapeutic range for 2 consecutive days.	Discontinue LMWH and commence dabigatran 0-2 hours before the time that the next dose of LMWH would be due.	Discontinue LMWH and commence edoxaban at the time that the next dose of LMWH would be due.	Discontinue LMWH and commence rivaroxaban 0-2 hours before the time that the next dose of LMWH would be due.	Discontinue LMWH and commence apixaban at the time that the next scheduled dose of LMWH would be due.	

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Guidelines adapted for local implementation across Hertfordshire from The East of England Priorities Advisory Committee, Atrial fibrillation anticoagulant clinical decision aid v3.1.

Prescriber Decision Support for Anticoagulating Patients with non-valvular AF Flow diagram adapted from AF (non-valvular): prescriber decision support for anticoagulation, Nottinghamshire Area Prescribing Committee.

Version

Version	3.0 Hertfordshire and West Essex guidelines for oral anticoagulation
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