The East of England
Priorities Advisory Committee
A function of PrescQIPP

PAC - Atrial fibrillation anticoagulant clinical decision aid

Contents

Atrial fibrillation anticoagulant clinical decision aid

Date		**Patient name**	
Age		**NHS number**	

CHA_2DS_2Vasc score*[1]		**HAS-BLED score*[1]**	
Annual stroke risk*[1]		**Annual bleed risk*[1]**	
Modifiable risk factors*[2]			
Contra-indications to anticoagulation*[2]			

***[1]** See page 3 and atrial fibrillation patient information and decision aid

*[2] See page 4

Clinical screening checklist

	U&Es (creatinine)	Weight (kg)*	FBC	LFTs	Baseline clotting	BP
Baseline (all patients)						

*Recent weight, ideally at time of clinical screening

Creatinine clearance (CrCl) Using Cockcroft & Gault formula. See page 10.	

Choice of anticoagulant

Warfarin		**NOAC**		**Referral**	

See pages 5 and 6 and table of NOAC comparisons.

Choice of NOAC		See page 7
Interactions with patient's current medicines		See drug interactions with NOACs
Dose		See page 9
Patient counselling		See appendix 1 – NOAC patient counselling checklist

Ongoing monitoring required

U&Es (creatinine)	Weight (kg)	FBC	LFTs	BP	See page 11

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

Online calculators are available on GP clinical systems

CHA_2DS_2Vasc scoring system for AF stroke risk[1,2,3]	
Risk factor	**Score**
Congestive heart failure/LV dysfunction	1
Hypertension	1
Age ≥ 75	2
Diabetes mellitus	1
Stroke/TIA/systemic arterial embolism	2
Vas**c**ular disease (previous MI, peripheral arterial disease, aortic plaque)	1
Age 65 -74	1
Sex (male 0, female 1)	F 1
Total score (maximum score 9)	

HAS-BLED score for bleeding risk[1,2,3]	
Risk factor	**Score**
Hypertension (uncontrolled, >160mmHg systolic)	1
Chronic liver disease or Bilirubin 2xULN with AST/ALT/ALP 3xULN	1
Abnormal renal function (creatinine ≥200micromol/L, renal transplant or chronic dialysis)	1
Stroke	1
History of major bleeding* or predisposition	1
Labile INRs, time in range less than 60%	1
Elderly (age ≥ 65 or frail condition)	1
Drugs (e.g. concomitant antiplatelet, NSAIDs) or alcohol (≥8 drinks/week) (1 point each)	1 or 2
Total score (maximum score 9)	

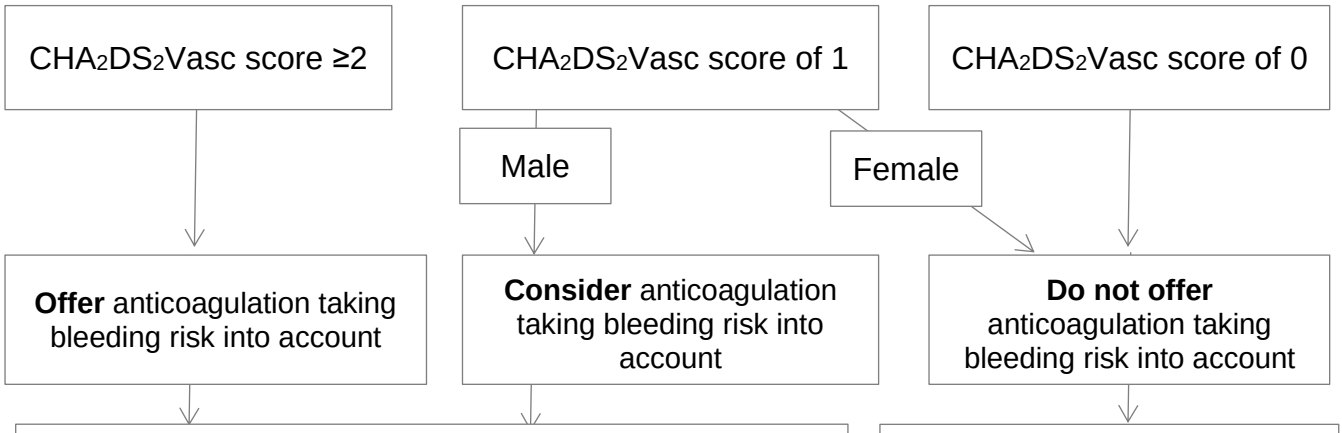
*Bleeding requiring hospitalisation and/or causing decrease in HB > 20g/L and/or requiring ≥ 2 units of blood transfusion.

Interpreting CHA_2DS_2Vasc and HAS-BLED score

CHA_2DS_2 Vasc score	**Events per 100 patients/year**	
	Stroke/TIA/ peripheral emboli	**Ischaemic stroke**
0	0.3	0.2
1	1.0	0.6
2	3.3	2.5
3	5.3	3.7
4	7.8	5.5
5	11.7	8.4
6	15.9	11.4
7	18.4	13.1

HAS-BLED score	**Major bleeding events per 100 patients/year in anticoagulation users**
0	-
1	0.7
2	1.9
3	2.4
4	3.4
5	5.7

Prescriber decision support for anticoagulating patients with non-valvular AF[1]



For most people benefit of anticoagulation outweighs bleeding risk.

Discuss in conjunction with Atrial fibrillation anticoagulation patient information and decision aid

For people with increased bleeding risk (e.g. HASBLED ≥3), address modifiable risk factors:

- Uncontrolled hypertension
- Concurrent medication (e.g. aspirin, NSAID)
- Harmful alcohol consumption
- Poorly controlled (labile) INRs

For people with an increased risk of bleeding the benefit of anticoagulation may not always outweigh the bleeding risk - careful monitoring of bleeding risk is important.

Do not withhold anticoagulation solely because the person is at risk of falls.

Patient is not a candidate for anticoagulation based on above assessment or patient refuses treatment:

Document outcome of assessment/patient decision in patient record.

Review annually, or when patient reaches 65 years or develops any of the following at any age:

- Hypertension
- Diabetes mellitus
- Heart failure
- Peripheral vascular disease
- Coronary artery disease
- Stroke/TIA/systemic arterial embolism

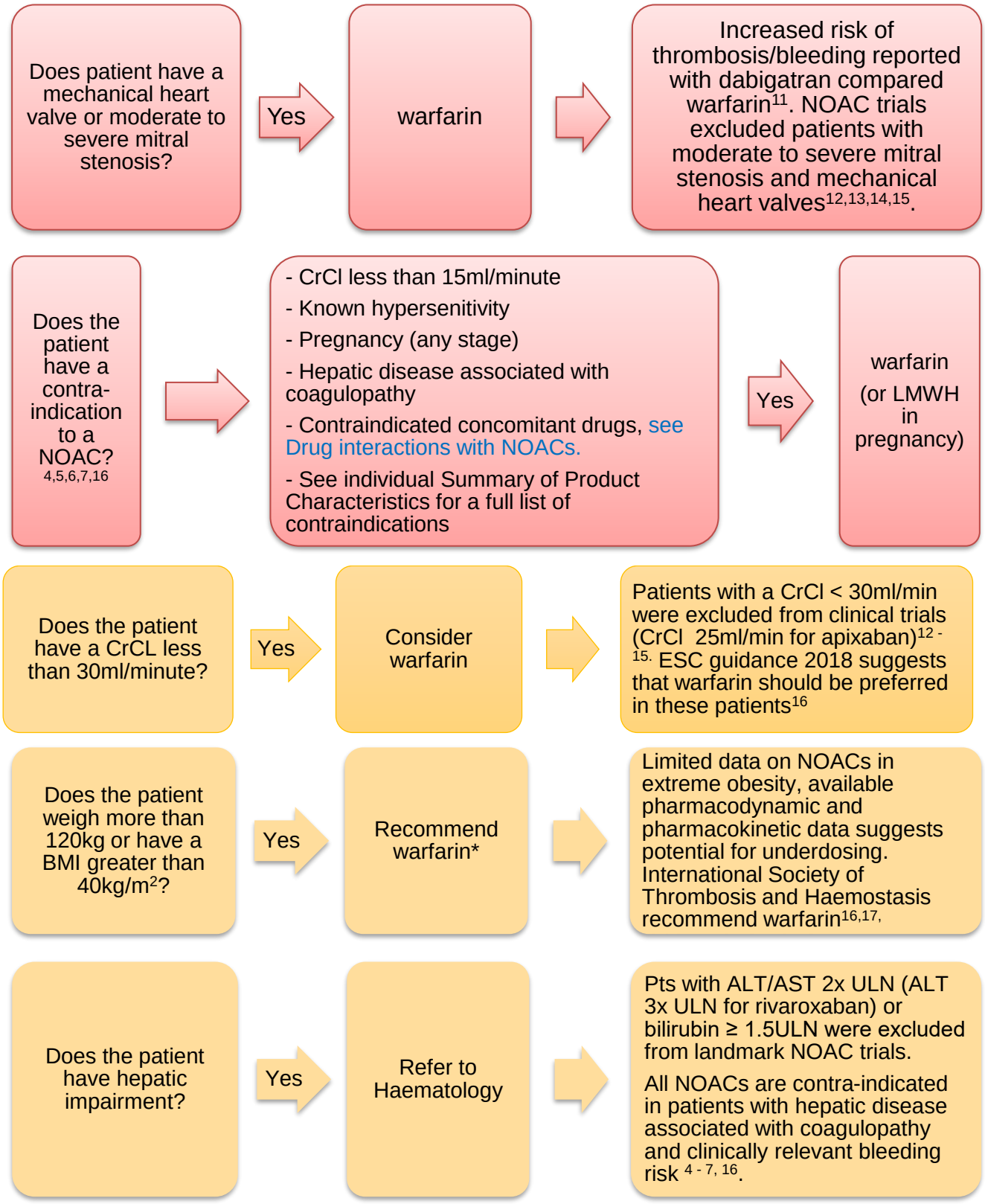
Contra-indications to anticoagulation[4-10]

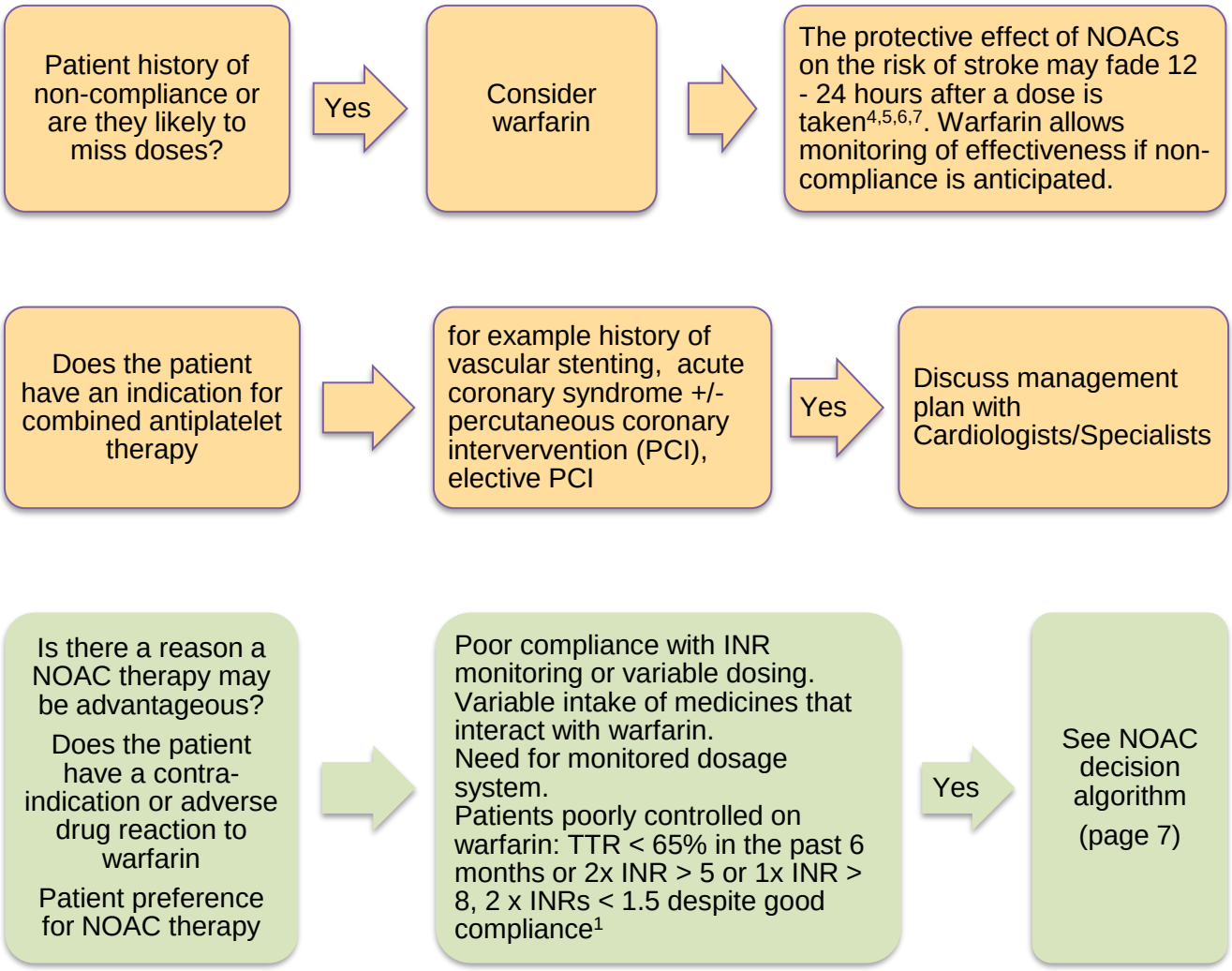
The following list of contraindications are taken from individual Summary of Product Characteristics (SPCs)[4-7], MHRA safety updates 20098 and 20139 and NICE CKS10. Discuss the clinical management plan with a Haematologist if there is a known contra-indication to anticoagulant treatment. The list below is not exhaustive; see individual SPCs for additional contraindications for individual anticoagulants, https://www.medicines.org.uk/emc:

- 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
- Concomitant treatment with any other anticoagulant

Choice of oral anticoagulant based on patient characteristics

Patients should already have been screened for an absolute contraindication to oral anticoagulation (see page 4).



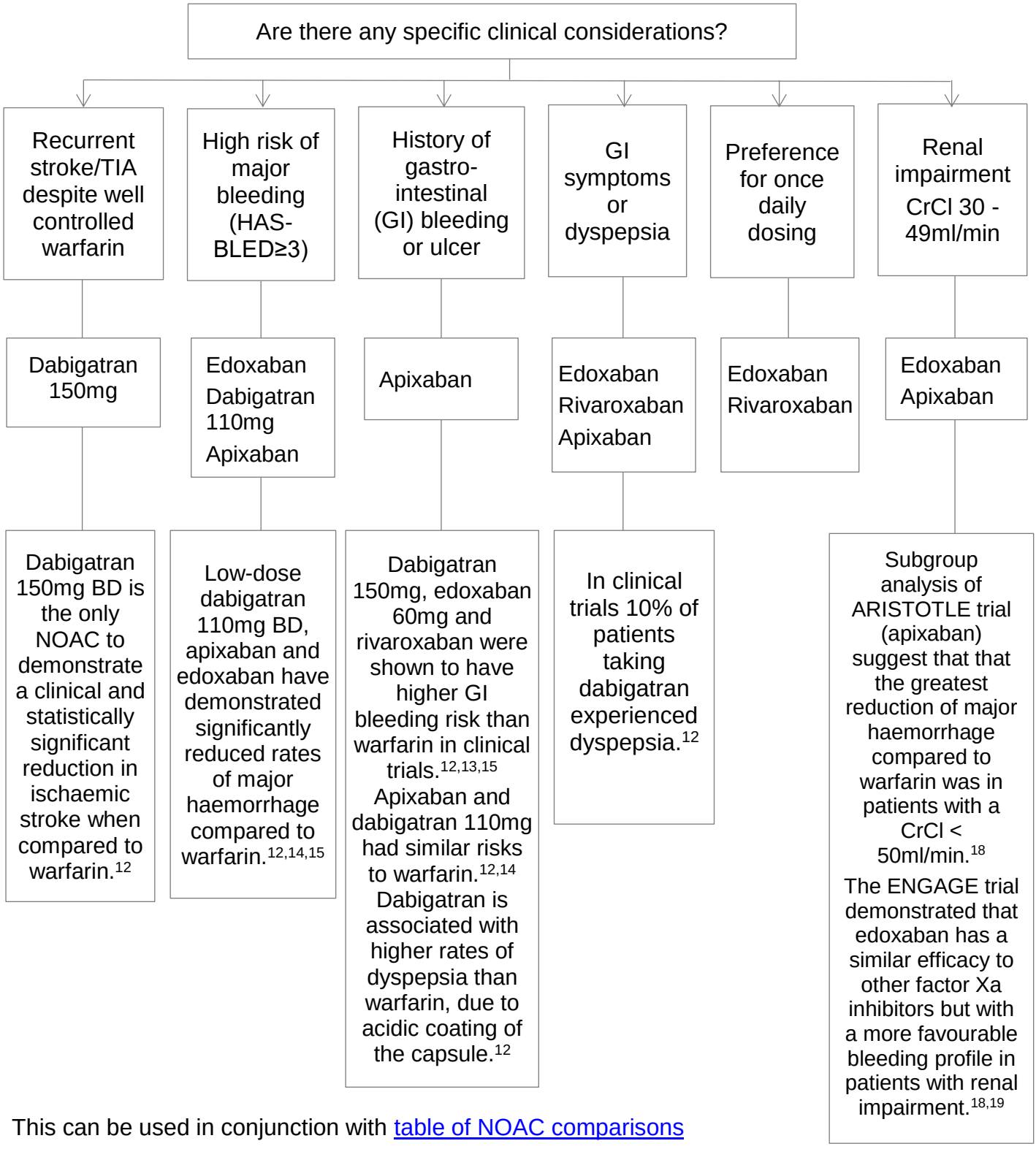


*The choice anticoagulant for obese patients over 120kg should be discussed with the patient. If a NOAC appears the best choice for a patient, refer to haematology as anti-Xa level monitoring may be required.

Choice of non-vitamin K oral anticoagulant (NOAC) based on patient characteristics

There have been no head-to-head trials between NOACs. The following is guidance is based on indirect comparisons. Detailed dosing advice can be found on page 9.

If there are no specific clinical considerations, use the NOAC of lowest acquisition cost. See local guidelines for NOAC of choice.



This can be used in conjunction with table of NOAC comparisons

Logical considerations

Need for a monitored dosage system	Edoxaban, apixaban, and rivaroxaban can be put in monitored dosage systems.	Dabigatran capsules should be stored in the original package in order to protect from moisture[4]
Swallowing difficulties or administration of medicines via enteral tube	Apixaban and rivaroxaban are licensed to be crushed, dispersed in water and administered via gastric tubes.[5,6] Edoxaban tablets can be crushed and administered either via a nasogastric tube or orally mixed in apple puree in patients who are unable to swallow solid oral dose formulations (unlicensed).[20]	Dabigatran capsules should not be opened as this leads to increased bioavalibility and potentially increased bleeding[4]

NOAC dosing for stroke risk reduction in non-valvular AF

Doses below are for stroke risk reduction in AF.

NB: 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

Alternatively refer to the Table of NOAC comparisons.

See page 10 for calculating creatinine clearance using the Cockcroft-Gault equation for NOAC dose calculation.

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.

Dabigatran[4]	Rivaroxaban[5]	Apixaban[6]	Edoxaban[7]
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: ○ ciclosporin, ○ dronedarone, ○ erythromycin, ○ ketoconazole

In general, as there is insufficent evidence for efficacy at lower doses for some agents, doses of NOACs should not be reduced unless a dose reduction is clinically indicated as outlined in the table above.

* A trend towards decreasing efficacy with increasing creatinine clearance was observed for edoxaban compared to well-managed warfarin. Therefore, edoxaban should only be used in patients with NVAF and high creatinine clearance (CrCl > 95ml/min) after a careful evaluation of the individual thromboembolic and bleeding risk.[7] In patients with CrCl > 95ml/min, rivaroxaban has shown numerically, but not statistically significant higher rates of stroke or systemic embolism per 100 patient years compared to warfarin.[21] There have been no peer-reviewed phase 3 sub analyses of the efficacy or safety of apixaban or dabigatran compared with warfarin in patients with a CrCl > 95ml/min.[18]

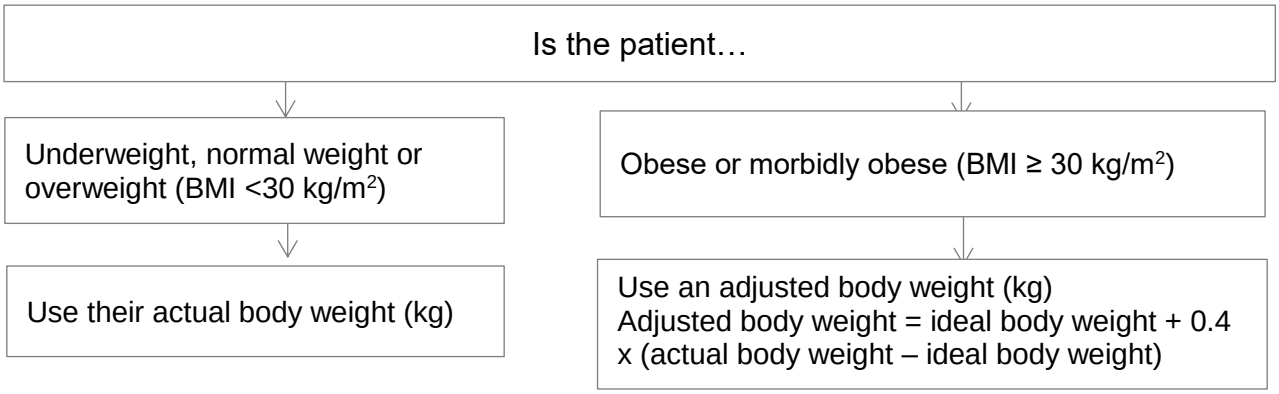
Calculating renal function – Cockroft and Gault (C&G) formula

The Cockcroft-Gault (C&G) equation is recommended by the manufacturers of all NOACs for calculating creatinine clearance (CrCl) when prescribing these agents.[4-7] **eGFR should not be used**, as data suggest it may lead to inappropriate dosing in up to 50% of patients.[22]

Cockroft and Gault equation for calculating CrCl

$$\text{CrCl (ml/min)} = \frac{(140\text{-age}) \times \text{weight*}}{\text{Serum creatinine (micromol/L)}} \times 1.23 \text{ (male) or } 1.04 \text{ (female)}$$

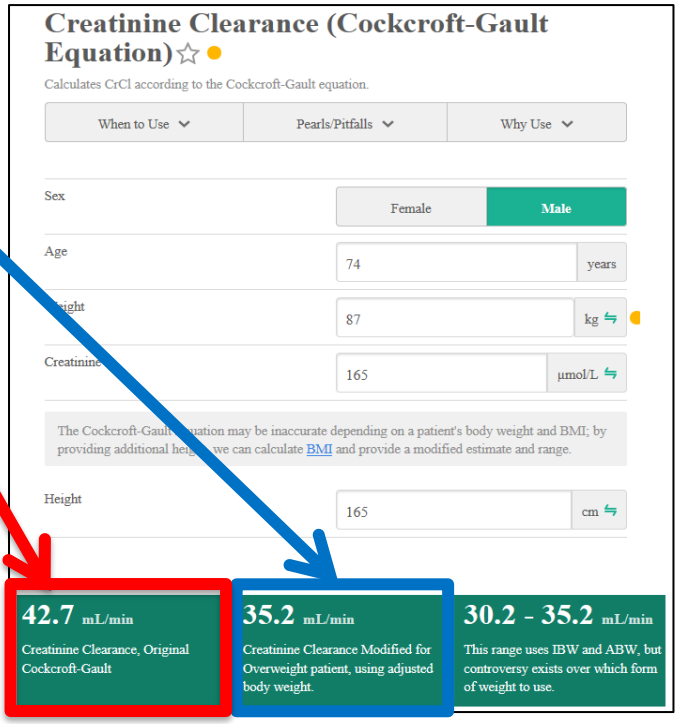
When calculating CrCl follow the guidance below



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

On the dose calculator this box will calculate a CrCl based on a patient's adjusted body weight (ABW)

On the dose calculator this box will calculate a CrCl based on a patient's actual body weight.



Where a patients CrCl places them on the cusp of a dose change it may be particularly important to consider other risk factors such as stroke, bleeding risk, co-morbidities and drug interactions before making a decision.

***Weight:** The clinical trials of NOACs used actual body weight when estimating CrCl for patients. However the number of patients with obesity within the NOAC 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 obese or morbidly obese (BMI ≥ 30 kg/m^2) patients estimate the CrCl range using adjusted body weight (ABW). 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.

NOAC monitoring and follow-up[10,16]

All patients on long-term anticoagulants require a general review at least once a year:

- Assessment of Stroke and Bleeding Risk
    - Recalculate CHA_2DS_2-VASc and HAS-BLED scores 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
- Assess adherence
    - Re-educate on importance of strict intake schedule
    - Identify any side effects, especially those that may be impacting on compliance
- Co-medications
    - Review other medications (inclusive of OTC and herbal medication) for drug interactions
    - See Drug Interactions with NOACs: https://www.prescqipp.info/our-resources/bulletins/bulletin-183-anticoagulation/
- Blood sampling and weight
    - Frequency of follow-up blood tests and weight[10,16]

Patient group	**U&Es**	**Weight**	**CrCl**	**FBC**	**LFTs**	**BP**	**Clotting**
Baseline (all patients)	Yes	Yes	Yes	Yes	Yes	Yes	Yes
CrCl > 60ml/min	Annually	Annually	Annually	Annually	Annually	Annually	INR will not provide information on intensity of anticoagulation effect. INR results for patient on NOACs do not correlate with clinical effect.
Any of the following: **Age ≥ 75 years, frail, CrCl 30 - 60ml/min**	6 monthly	6 monthly	6 monthly	Annually	Annually	Annually	
CrCl < 30ml/min or an expected decline in renal function	3 monthly	3 monthly	3 monthly	Annually	Annually	Annually	
Intercurrent condition that may impact renal or liver function	If needed	If needed	If needed	If needed	If needed	If needed	

- Reassess based on the above whether:
    - The chosen NOAC/OAC is the best for the patient
    - The chosen dose is correct

Warfarin monitoring and follow-up

All patients on long term anticoagulants require a general review at least once a year:

Assessment of Stroke and Bleeding Risk

- Recalculate CHA_2DS_2-VASc and HAS-BLED scores 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

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 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.

Appendix 1: NOAC 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[4-7, 16]	√
Explain purpose.	
Dose and frequency.	
Timing of doses. Ensure that rivaroxaban is taken with food.[3]	
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 NOAC if prescribed new medications or surgery /or if invasive procedures (including dental extractions) being planned. Bleeding risk if NOAC 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[4-7,10,16]

Consult the Summary of Product Characteristics for each individual anticoagulant for further information.

INR values may be falsely elevated after the intake of NOACs

Switching from	Switching to					
	Warfarin	**Dabigatran (Pradaxa)**	**Edoxaban (Lixiana)**	**Rivaroxaban (Xarelto)**	**Apixaban (Eliquis)**	**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 NOACs				
Dabigatran (Pradaxa)	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.

Switching from	Switching to					
	Warfarin	**Dabigatran (Pradaxa)**	**Edoxaban (Lixiana)**	**Rivaroxaban (Xarelto)**	**Apixaban (Eliquis)**	**Low Molecular Weight heparin (LMWH)**
Edoxaban (Lixiana)	**Patients on 60 mg dose of edoxaban;** administer edoxaban at a dose of 30 mg once daily together with warfarin. **Patients on 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 (Xarelto)	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 (Pradaxa)**	**Edoxaban (Lixiana)**	**Rivaroxaban (Xarelto)**	**Apixaban (Eliquis)**	**Low Molecular Weight heparin (LMWH)**
Apixaban (Eliquis)	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.
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.	

Document history

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Consultation Process	East of England Clinicians		
QA Process	Katie Smith, Senior Clinical Pharmacist, PrescQIPP. 14th February 2019		

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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 https://www.nottsapc.nhs.uk/media/1043/anticoagulants-in-af.pdf

Calculating Renal Function – Cockcroft & Gault (C&G) Formula. Section adapted from South London Calculating Creatinine Clearance for DOACs.

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