NHS
Lincolnshire
Integrated Care System

Anticoagulation guidance for Non-Valvular Atrial Fibrillation (NVAF)

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Source
(Adapted from UKCPA/PCCS/PCPA July 2022)

Version	Authors	Last Reviewed	Next Review date
1	Clinical Pharmacists Medicines Optimisation Team LICB in collaboration with: Clinical pharmacists ULHT (cardiology/renal) Consultant cardiologists GP Leads PCN Clinical pharmacists Guidance circulated to other consultants for feedback including specialists in stroke	Oct 2023	
2	Clinical Pharmacist Medicines Optimisation Team (update Apixaban status; new SPS interactions page)	Jan 2024	Jan 2025

Contents

Introduction

These guidelines cover the use of anticoagulation for paroxysmal, persistent, and permanent AF and atrial flutter. Do **not** use this guideline for patients with pulmonary embolism, deep vein thrombosis, significant structural heart disease, congenital heart disease or cardiomyopathy. Refer patients promptly at any stage if treatment fails to control the symptoms of AF and more specialized management is needed. NICE define "promptly" as within four weeks of failed treatment. The diagnosis and management of NVAF is beyond the scope of this guidance and prescribers should refer to the appropriate NICE guidance.

Prevalence and Risk

NVAF is currently the most common heart rhythm disturbance, with an estimated overall population prevalence in England of 2.5%. NICE CKS refers to a large meta-analysis carried out in 2016 that found AF was associated with a 46% increase in all-cause mortality. There is a significantly increased risk of ischaemic heart disease, chronic kidney disease, sudden cardiac death, and heart failure, a 96% higher risk of a major cardiovascular event, a two-fold increase in cardiovascular mortality, and a 2.3-fold increased risk of stroke. **Anticoagulation treatment reduces the risk of stroke by about two-thirds.**

A cohort study of the incidence of AF and direct oral anticoagulant (DOAC) prescribing from 2009 to 2019, found the incidence of NVAF had increased in the past decade and there were inequalities in prescribing of DOACs due to clinical and sociodemographic factors. As untreated AF is a significant risk factor for stroke and thromboembolic events, NHS England has developed a new infographic in support of the national initiative to expand the use of DOACs, accelerating treatment and improving AF related outcomes in England.

DOAC comparison

NICE have not distinguished between any of the four DOACs with UK marketing authorisation. There are no published head-to-head trials comparing one DOAC to another that can be used to confer superiority between the DOACs. The population differences between the trials comparing each DOAC to warfarin were large making it difficult to draw any conclusions between any inferred advantages. A meta-analysis in NICE TA 355 showed all high dose DOACs have comparable efficacy for the composite end point of stroke and systemic embolism, but bleeding risk was significantly lower for Edoxaban and apixaban than those seen with dabigatran and rivaroxaban, although further trials are needed to confirm this in clinical practice.

The choice of anticoagulant in AF should be made with the patient and is dependent upon clinical features and preferences.

Although Edoxaban remains first line choice based on NHSE recommendations and the National Procurement for DOACs scheme, currently the most cost effective DOAC is Apixaban. The NHSE choice of DOAC could change in the near future to reflect this, although this is yet to be confirmed. There is no recommendation to switch patients currently on Apixaban to Edoxaban.

DOAC Choice and Lincolnshire guidance

The first line choice of DOAC for NVAF is Edoxaban, although there is no recommendation to switch patients prescribed Apixaban to Edoxaban, (unless it is more suitable for patient compliance) . This guidance has been developed in collaboration with both primary and secondary care (including local specialists e.g cardiologists, stroke physicians, as well as GPs, hospital and PCN clinical pharmacists).

The aim of the Lincolnshire guidance is to support prescribers with the choice and prescribing of suitable and cost-effective DOACS, also sometimes known as novel oral anticoagulants (NOACs) or non-Vitamin K anticoagulants, for the treatment of NVAF, as there are several treatment options available.

It includes the following:

- patient factors to consider when prescribing a DOAC.
- assessment of risk factors for anticoagulation including stroke and bleeding risk,
- monitoring requirements,
- guidance on prescribing for new patients
- switching from warfarin or another DOAC,
- a counselling checklist,
- some advice on management of problems
- information on management of dental patients.

Initiating Anticoagulation for non-valvular atrial fibrillation (NVAF)

Calculate stroke risk and bleeding risk. see appendix 2

Before initiation of any anticoagulation the following baseline parameters should be checked: Weight, FBC, U&E's, LFT's, Clotting screen and BP.

***Edoxaban should be used in patients with NVAF and high CrCl (≥ 95ml/min) only after a careful evaluation of the individual thromboembolic and bleeding risk.**

Patient requires oral anticoagulation for NVAF

↓ Yes

Are DOACS declined(informed choice) OR Contra-indicated (Mechanical heart valves, moderate – severe mitral stenosis, antiphospholipid syndrome)?

Yes → **Initiate warfarin with appropriate INR monitoring.**

A higher INR target may be required if mechanical heart valve/ antiphospholipid syndrome.

↓ No

Does the patient have a CrCl > 50ml/min but <95ml/min, and weight >60kg?

Yes → **Commence Edoxaban 60mg once daily.**

↓ No

Does the patient have a CrCl ≤ 50ml/min but ≥ 15ml/min?

Yes → **Commence Edoxaban 30mg once daily.**

↓ No

Does the patient weigh ≤60Kg?

Yes → **Commence Edoxaban 30mg once daily.**

↓ No

Is the patient taking regular ciclosporin, dronedarone, erythromycin, or ketoconazole (see SPC for further drug interactions*)

Yes → **Consider alternative DOAC in line with SmPC* criteria e.g rivaroxaban 20mg once daily.**

↓ No

Does the patient have a CrCl ≥ 95ml/min?

Yes → **Counselling checklist and Patient Resources-** appendix 6 and 7

Management Dental Patients – appendix 8

↓ No

Does the patient have a CrCl <15ml/min or are they on dialysis?

↓ Yes

Consider the risk and benefit situation in severe renal dysfunction where bleeding risk is elevated.

↓

Does the patient wish to receive oral anticoagulation after discussion of benefits and risks?

Yes → **Initiate warfarin with INR range 2.0-3.0**

Adapted from UKCPA/PCCS/PCPA:Initiating anticoagulation for NVAF following NHSE DOAC commissioning recommendations July 2022

*https://www.medicines.org.uk/emc/product/6905/smpc

Anticoagulation Choice – See appendix 1

DOACs should be used first line for NVAF, exclusions include:

- Mechanical heart valves (or within 3 months of bioprosthetic tissue valve)
- Moderate to severe mitral valve stenosis
- Antiphospholipid syndrome.
- Renal Failure with creatine clearance <15mls/min
- Patient requiring a higher INR range (>2-3)
- Concomitant use of drugs which are contradicted with DOACS – see SmPCs

DOAC monitoring -see appendix 3

DOACs are not without a need for surveillance as their dosing is determined by renal function
Recommended renal monitoring frequencies:

- Creatinine Clearance >60mls/min Routine surveillance every 12 months
- Creatinine Clearance 30-60mls/min. Routine surveillance minimum every 6 months
- Patients over the age of 75 years and / or frail. Routine surveillance every 6 months
- Creatinine Clearance 15-30ml/min. Routine surveillance minimum every 3 months
- More frequent monitoring is recommended if there has been a significant recent decline in renal function – see appendix 3 for details.

Calculation Creatinine Clearance (CrCl)- see appendix 5

Creatinine Clearance ≤15mls/min

When creatinine clearance has fallen to <15mls/min, DOAC should be discontinued. Warfarin can be used in those with poor renal function following appropriate discussion regarding stroke and bleeding risk. Alternatively, a left atrial appendage occlusion (LAAO) device could be considered in line with NICE guidance.

LAAO - If a patient has significant risk of AF related cardioembolic stroke but cannot receive an oral anticoagulant either due to renal function or bleeding, consider referral to cardiology for consideration of LAAO device insertion.

More information can be found about this at the AF Association Left-Atrial Appendage Occlusion.

Information on switching from Warfarin to a DOAC

It is for the prescribing clinician to determine which DOAC(s) are clinically appropriate for an individual patient based upon the relevant NICE technology appraisal guidance.

When switching to a DOAC, care should be taken to follow the recommendations in the relevant SPC:

- 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

A switch from warfarin to a DOAC should not be considered for patients:

- With a prosthetic mechanical valve
- With moderate to severe mitral stenosis
- With antiphospholipid antibody syndrome (ALS) (except were advised by an anticoagulant specialist)
- Who are pregnant breast-feeding or planning a pregnancy
- Requiring a higher INR than the standard INR range of 2.0 – 3.0
- With severe renal impairment - Creatinine Clearance (CrCl) < 15ml/min
- With venous thrombosis at unusual sites (e.g., portal vein thrombosis)
- **Any patient who is currently under active care of the cardiology service without prior discussion with the initiating consultant.**

Seek advice for patients with:

- Active malignancy/ chemotherapy
- Prescribed interacting drugs – check SmPCs for full list.
- Some HIV antiretrovirals and hepatitis antivirals - check with HIV drug interactions website at https://www.hiv-druginteractions.org/
- Some antiepileptics- phenytoin, carbamazepine, phenobarbitone or rifampicin are likely to reduce DOAC levels so should be discussed with an anticoagulation specialist.
- On triple therapy (dual antiplatelet therapy plus warfarin)

Suggested process for safe switching from warfarin to a DOAC:

1. Check recent U&Es, LFTs and FBC (ideally within the last 3 months) and calculate creatinine clearance (see appendix 5), using actual body weight from last 12 months (unless recent weight loss/gain).
2. Check INR
3. Discuss options with your patient and/or carers (as appropriate) and, with consent, prescribe DOAC at appropriate dose – Edoxaban preferred first-line: see overleaf.
4. **Remove warfarin from the repeat prescription after initiating DOAC**
5. 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 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=e7e62356-8aa6-472a-aeb1-eb5b58315d49

6. 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.
7. Provide an up-to-date Anticoagulant Alert and DOAC counselling (see checklist)
8. Where the switch to a DOAC is undertaken outside the GP practice, provide accurate information relating to indication, baseline tests and monitoring requirements to allow primary care to safely take over prescribing responsibility.
9. Inform community nursing teams if they have been monitoring INR or administering warfarin
10. Ensure appropriate on-going monitoring is in place using the clinical system recall function – frequency will depend on renal function, age, and frailty

Information on switching from another DOAC to Edoxaban

It is for the prescribing clinician to determine which DOAC(s) are clinically appropriate for an individual patient based upon the relevant NICE technology appraisal guidance.

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

Do NOT switch from another DOAC to Edoxaban:

•any patient who is currently under active care of the cardiology service without prior discussion with the initiating consultant.

•Where a patient is not likely to comply with changes.

Patients in whom a switch to Edoxaban may be less suitable (see also contraindications and cautions in SmPC: https://www.medicines.org.uk/emc/product/6905/smpc

•Other indications for anticoagulation, such as venous thromboembolism (DVT or PE) within the last 6 months

•Unlicensed indications eg left ventricular thrombus, portal vein thrombosis, arterial thrombus, antiphospholipid syndrome (APS), short term use, such as pre/post cardioversion

•Recent CV event (acute coronary syndrome or stent insertion) prescribed single or dual antiplatelet therapy with a DOAC

•Where a specialist has indicated a clinical reason for using a specific DOAC

•Recent major bleed* or new major bleeding risk)* or interacting drugs which increasing bleeding risk (for example; ciclosporin, dronedarone, erythromycin, or ketoconazole)

•History of severe menorrhagia*

•Active malignancy or chemotherapy

•Extremes of bodyweight: > 120kg (or BMI > 40) or < 50kg

•Hepatic disease associated with coagulopathy and significant bleeding risk*

•Haemoglobin (Hb) <10g/dL or Platelets <100 (x109/L) - investigate and address underlying causes*

•Cognitive dysfunction – if there are concerns regarding patient understanding

•Recent falls / increasing frailty*

***Review whether on-going anticoagulation therapy is safe / appropriate**

Suggested process for each patient:

1. Check recent U&Es, LFTs and FBC (ideally within the last 3 months) and calculate creatinine clearance (see appendix 5) 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 - see overleaf.
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 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****
Start new drug when dose of previous drug would have been due. Patients must not be on more than one drug at once.

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. Where the DOAC switch is undertaken outside the GP practice, provide accurate information to allow primary care to safely take over prescribing responsibility.
9. Inform community pharmacy of the change and encourage follow up via new medicines service or discharge medicines service
10. Ensure appropriate on-going monitoring is in place using the clinical system recall function – frequency will depend on renal function, age, and frailty.

DOAC Prescribing for Non-Valvular AF (NVAF)

*see product SPC for full details

DOAC	Edoxaban (FIRST choice)	Rivaroxaban	Apixaban (*see p4 and p5 for local guidance on use)*	Dabigatran
Dosing in Non-valvular AF (lifelong unless risk: benefit of anticoagulation therapy changes)	Prescribe Edoxaban 60mg once daily. **Reduce dose to 30mg once daily if following apply:** Body weight ≤60kg, OR CrCl≤ 50ml/min but ≥15ml/min , OR co-prescribed with ciclosporin, dronedarone, erythromycin or ketoconazole.	Prescribe Rivaroxaban 20mg once daily. **Reduce dose to 15mg once daily if following apply:** CrCl< 50mL/min in NVAF patients only.	Prescribe Apixaban 5mg twice daily. **Reduce dose to 2.5mg twice daily if following apply:** At least two of the following characteristics: age ≥ 80 years, body weight ≤ 60 kg, or serum creatinine ≥ 133 micromol/l or if exclusive criteria of CrCl 15 - 29 ml/min.	Prescribe Dabigatran 150mg twice daily if aged <75 years, CrCl> 50mL/min, low risk of bleeding (weight <50kg with close clinical surveillance) **Reduce dose to 110mg twice daily if following apply:** Aged > 80 years or prescribed verapamil. Consider 110mg twice daily based on individual assessment of thrombotic risk and the risk of bleeding in patients aged between 75 and 80 years or with CrCl <50mL/min or with increased risk of bleeding (including gastritis, esophagitis, gastro-esophageal reflux).
Contraindicated / Not Recommended *	CrCl <15ml/min	CrCl <15ml/min	CrCl <15ml/min	CrCl <30ml/min
Cautions*	CrCl ≥95ml/min- consider alternative DOAC **(Careful evaluation bleeding and thromboembolic risk)**	CrCl <30ml/min. Take with or after food (15mg and 20mg doses).		Do not use in a standard medication compliance aids (MCA)
Interactions **Affected by drugs that are strong inhibitors/inducers of both CYP3A4 and P-GP pathways, for individual DOAC details check:** **Check BNF:** **www.bnf.org** **SPC:www.medicines.org.uk**	Rifampicin, Phenytoin, Carbamazepine, Phenobarbital or St. John's Wort – use with caution. Ciclosporin, dronedarone, erythromycin, ketoconazole – reduce dose as above. (See BNF and SPC for edoxaban for further information)	Ketoconazole, itraconazole, voriconazole, Posaconazole, ritonavir, dronedarone – not recommended (See SPC for full details) Rifampicin, phenytoin, carbamazepine, phenobarbital, St. John's Wort – Should be avoided.	Ketoconazole, itraconazole, voriconazole, Posaconazole, ritonavir - not recommended (See SPC for full details) Rifampicin, phenytoin, carbamazepine, phenobarbital, St. John's Wort – use with caution. Do not use apixaban with patients on strong enzyme inducers for acute VTE treatment	Ketoconazole, ciclosporin, itraconazole, tacrolimus, dronedarone - contraindicated (See SPC for full details) Rifampicin, St John's Wort, carbamazepine, phenytoin – should be avoided. Amiodarone, quinidine, ticagrelor, Posaconazole – use with caution. Verapamil (use reduced dose). Antidepressants: SSRIs and SNRIs- increased bleeding risk

Further information:

Anticoagulant Suggestions for adults with Swallowing difficulties Specialist Pharmacy Service (SPS); Oral Anticoagulants during Breastfeeding (SPS)

Interactions Edoxaban | Interactions | BNF | NICE ; Managing interactions with direct oral anticoagulants (DOACs) (SPS); Non-vitamin K antagonist oral anticoagulants (NOACs): Is it safe to take them with herbal medicines? (SPS);Chondroitin – what are its drug interactions? (SPS)

APPENDIX 1: Considerations when choosing oral anticoagulant.

NICE recommends that the decision to start treatment should be made after an informed discussion between the patient and clinician on the risks and benefits of treatment selected. See Information for the public | Atrial fibrillation: diagnosis and management | Guidance | NICE for more information and the counselling section in the guidance for patient decision aids which can be used to support such discussions.

Patient Factors	Outcome	Preferred Treatment Options
Does patient prefer a once daily formulation? (Consider concordance, reliant on carers/ nursing visits)	**Y**	**Edoxaban** – can be given as once daily dose. **Warfarin** – given as a single dose but may be necessary to give several tablets dependent on dose. **Rivaroxaban** - can be given as a single dose with food.
Does the patient require medication in a compliance aid?	**Y**	**Edoxaban** – no special storage requirement. Stable outside of original packaging for 3 months. **Warfarin** - can be used in compliance aid as long as risk assessment has been undertaken and a management plan in place to manage dose changes. **Apixaban** – no special storage requirement can be used in compliance aid. **Rivaroxaban** – no special storage requirement can be used in compliance aid. Dabigatran- not suitable for compliance aid as it is sensitive to moisture.
Does the patient have swallowing difficulties?	**Y**	**Edoxaban** Swallowing difficulties - Tablets can be crushed and mixed in water or mixed in apple puree/sauce. Enteral tubes - Tablets can be crushed and mixed with water for administration. **Rivaroxaban** Poor oral intake or inability to take with food can cause treatment failure with rivaroxaban. Swallowing difficulties - Can be crushed and mixed with water or apple puree immediately before use and administered orally. Gastric tube - May be given through a nasogastric tube after confirmation of the correct placement of the tube. The crushed tablet should be administered with a small amount of water via a gastric tube after which it should be flushed with water. (Rivaroxaban should not be administered through feeding tubes that do not terminate in the stomach. This includes NJ, PEJ, and PEGJ tubes) **Apixaban** Swallowing difficulties - Tablets can be crushed and mixed with water, glucose 5%, apple juice or apple puree. Take care to ensure the whole dose is administered. Enteral tubes - Tablets can be crushed and dispersed in water or in glucose 5% for administration. Licensed for administration through nasogastric tubes. Take care to ensure the whole dose is administered and flush well after each dose. **Please note Dabigatran capsules must not be opened as it results in a substantial increase in drug bioavailability (+75%)**

Patient Factors	Outcome	Preferred Treatment Options
Is the patient likely to miss doses?	Y	Preferred option warfarin unless compliance aid assists compliance (see above) **Warfarin -** Patients with poor concordance may be at greater risk of thromboembolic complications with DOACs as the shorter half-lives of these agents compared to warfarin will potentially result in more time without any degree of anticoagulation if a dose is missed.
Is the patient needle phobic?	Y	**DOACs - Edoxaban (formulary choice)** Although there is no need for regular blood tests to monitor INR, people taking DOACs still require regular follow-up. When initiating treatment baseline tests will be needed to be performed and patients monitored on a regular basis at least annually, however less than warfarin. Warfarin – requires frequent monitoring, at least every 3 months. (Near patient testing only requires capillary blood – finger prick)
Does the patient have a BMI>40 or weight>120kg <50kg?	Y	**>120kg** **Warfarin -** No dose adjustment on weight **DOACs –** The International Society of Thrombosis and Haemostasias (ISTH) does not recommend using DOACs in patients above 120Kg unless levels are measured – which would need to be in secondary care setting. **<50kg** will be at increased bleeding risk. Choose the most appropriate licensed dose DOAC for patient taking into account history and co-morbidities consider monitoring levels/ warfarin for high bleeding risk.
Is it important to have 24 hour coverage?	Y	**DOACs –** Apixaban twice daily dosing is considered more favorable in this situation. **Edoxaban** - a single dose administered as per the SmPC would also provide over 24-hour anticoagulation.
Does the patient have a Renal Impairment?	Y	See guidance below or SPC for details of contra-indications and dosing
High CrCl ≥95ml/min?	Y	**Edoxaban –** shows decreased efficacy at high creatinine clearance Patients already established on edoxaban and later found to have a CrCl ≥95ml/min, should have their anticoagulation plan reviewed (and possibly *switch onto an alternative DOAC such as Rivaroxaban)*
Regular courses erythromycin or fluconazole	Y	Patients on these drugs that may not be able to comply with taking reduced doses for fixed periods, may not be suitable for Edoxaban
Other patient conditions	Y	**Seek specialist advice for:** • Heart failure patients with fluid overload • Patients with extensive amputations (also see section below on estimating weight), or neurological diseases (e.g., spina bifida, multiple sclerosis) and myopathy that may result in profound muscle loss • Post surgery, • Any patients under cardiologist care • Chemotherapy/ active malignancy • Abnormal uterine bleeding • Recent PE or DVT in past 6 months
Already on DOAC (not Edoxaban)?	Y	If started by specialist or in secondary care and no reason documented, check rationale with prescriber and document. If no rationale, discuss switch to edoxaban if other clinical and patient factors are suitable. No requirement to switch patients already on Apixaban, unless issues with patient compliance.
Already on aspirin or other antiplatelet?	Y	Seek specialist advice.

APPENDIX 2: Assessment of Risk Factors for Anticoagulation

Stroke and bleeding risk should be assessed in all patients with AF.

1.Stroke risk

Use CHA2DS2-VASc Score to assess stroke risk in people with:

• Symptomatic or asymptomatic paroxysmal, persistent, or permanent atrial fibrillation
• Atrial flutter
• A continuing risk of arrhythmia recurrence after cardioversion back to sinus rhythm (cardiologist decision or CHADSVASC≥2) or catheter ablation.

CHA2DS2-VASc score	Anticoagulation	Action
0	Do NOT offer anti-coagulation	• Review annually • Review patients not taking any anticoagulants when they reach age of 65 or if they develop any of the following at any age: - Diabetes - HF - Peripheral arterial disease - coronary heart disease - Stroke, TIA, or systemic thromboembolism. • Do **not** offer aspirin monotherapy for stroke prevention, however patients already on antiplatelets for another indication may continue.
1	Men – consider DOAC taking into consideration bleeding risk** Women- do **not** offer DOAC	For men only: Discuss options for anticoagulation based on patient factors and clinical features. * **Edoxaban is first line formulary choice for patients with NVAF**
≥2	Offer DOAC taking into account bleeding risk**	Discuss options for anticoagulation based on patient factors and clinical features. * **Edoxaban is first line formulary choice for patients with NVAF**

**** see assessment of bleeding risk and modifiable risk factors below**

*NICE recommend when discussing the **benefits and risks of anticoagulation**, explain that:

• For most patients the benefit of anticoagulation outweighs the bleeding risk
• For people with an increased risk of bleeding, the benefit of anticoagulation may not always outweigh the bleeding risk and careful monitoring of bleeding risk is important.
• Do not withhold anticoagulation solely because the person is at risk of having a fall, (consider specialist opinion).
• Do not offer aspirin (or clopidogrel) monotherapy solely for stroke prevention to people with AF.
• If considering or offering anticoagulation, offer a DOAC.
Where a DOAC is contraindicated, not tolerated or not suitable in people with atrial fibrillation, offer a vitamin K antagonist. The clinician should discuss the options for anticoagulation with the patient and drug choice should consider clinical features, preferences, and bleeding risk.

Also refer to the counselling checklist and patient resources below.

2.Bleeding Risk**

Use the Orbit bleeding risk score (if available on clinical system), or HAS-BLED Score (if ORBIT is unavailable) to assess the risk of bleeding in patients on initiating or reviewing anticoagulants. This will also help when making a shared decision with the patient about whether to start anticoagulation, and about how to reduce modifiable risk factors for bleeds.

High Orbit Score or Bleeding risk

- Check haematinics and replace iron/folate/B12 if required.
- Consider a PPI (proton pump inhibitor)
- Review modifiable risk factors – see below.

Monitoring and support should be offered for **modifiable risk factors of bleeding risk** such as:

- uncontrolled hypertension (see NICE's guideline on hypertension in adults)
- poor control of international normalized ratio (INR) in patients on vitamin K antagonists
- concurrent medication, including antiplatelets, selective serotonin reuptake inhibitors (SSRIs) and non-steroidal anti-inflammatory drugs (NSAIDs)
- harmful alcohol consumption (see NICE's guideline on alcohol-use disorders: diagnosis, assessment and management of harmful drinking and alcohol dependence)
- reversible causes of anemia.

(See NICE CG 196 AF diagnosis and management updated 30.6.2021 Overview | Atrial fibrillation: diagnosis and management | Guidance | NICE

The decision to stop anticoagulation should be made based on a reassessment of stroke and bleeding risk and following a discussion of the person's preferences. Do not stop anticoagulation solely because atrial fibrillation is no longer detectable.

APPENDIX 3: Monitoring

Baseline: Before initiation of any anticoagulation the following baseline parameters should be checked: Weight, FBC, U&E's, LFT's, clotting screen and BP. Weight should be measured in order for calculated renal function to remain accurate. BP should be checked at the start and periodically as uncontrolled severe hypertension is a contra-indication to use, as there is a higher risk of bleeding.

Once treatment has started, review the person on a regular basis, preferably after 1 month initially and at least every 3 months thereafter. Follow-up intervals may be longer (up to every 6 months) or shorter (for example every month) depending on patient factors, such as renal function, age, and comorbidities, and co-prescribing of nephrotoxic drugs. Hypovolaemia and dehydration may affect renal function and warrant closer monitoring.

Annual weight, BP, LFTS + FBC +U+Es for most people. If frail or >75yrs check 6 monthly. Intercurrent illness check as needed. The SPS recommends more frequent testing if CrCl <60ml/min; divide CrCl by 10 to obtain the frequency of monitoring, for e.g CrCl 30ml/min monitor 3 monthly. See the following link for details.

APPENDIX 4: Management of problems at review

Problem	Action
Decline in renal function, but CrCl>30ml.	Review dose, assess bleeding risk.
Decline in renal function to <30ml/min with dabigatran, or <15ml/min with apixaban, rivaroxaban, Edoxaban.	Stop DOAC, assess bleeding risk and seek specialist advice.
Haemorrhage (e.g., GI bleed, head injury) *Unexplained* fall in BP *Unexplained* fall in haemoglobin and/or haematocrit.	Refer immediately to A+ E for investigation. Stop treatment with DOAC.
Excessive bruising.	Refer to haematologist.

**where significant decline in renal function, then recheck weight also to ensure accurate CrCl calculation*

APPENDIX 5: Calculation of Creatinine Clearance (CrCl)

For calculation of DOAC dose, do not use eGFR, use Creatinine Clearance (CrCl).

Use **"actual" body weight in the Cockcroft Gault equation to calculate the creatinine clearance (for body weight within the normal range, i.e up to an including 120kg**), as this was used to calculate CrCl in the clinical trials on DOACS. You can use the following link or calculate manually:

Cockcroft-Gault Equation

$$\text{Creatinine Clearance (ml/min)} = \frac{(140 - \text{Age}) \times \text{Weight (kg)}^{*} \times \text{constant}}{\text{Serum Creatinine (µmol/L)}}$$

Constant = 1.23 for male and 1.04 for female

Note: some clinical systems embedded in GP practices do not give a reliable estimate of CrCl. It is safer to calculate using the equation above or mdcalc. Do not use eGFR which can overestimate renal clearance especially in low body weight. If the embedded calculator in SystmOne is being used, the patient's height should be removed to prevent adjustments from actual body weight to ideal body weight within the calculator. Emis may give text information as to whether actual or ideal body weight has been used.

For estimating weight following amputation and presence of oedema and ascites see following link. Also seek specialist advice.

Extremes of body weight

There is national variation about which weight to use for CrCl calculations in obese patients, and currently there is no consensus.

It should be remembered that all values are estimates of renal function. Using ideal body weight may underestimate renal function, so when being used to dose DOACs may result in a risk of under coagulation. Conversely using actual body weight may overestimate renal function. Some regions also use adjusted body weight. Clinical judgement needs to be considered in these cases. Document the method used in the patient record**,** and consult specialist for advice.

The local recommendation is to use actual body weight for patients up to and including 120kg.

>120kg warfarin is recommended locally as there is limited clinical data on DOAC use in extremes of weight.

< 50kg patients will be at increased bleeding risk. Choose the most appropriate licensed dose DOAC for the patient taking into account history and co-morbidities, consider monitoring levels/ warfarin for those with a high bleeding risk.

Consult specialist for further guidance or if in doubt, also see appendix 1 (considerations on choosing an oral anticoagulant).

APPENDIX 6: Counselling checklist for DOAC's

Counselling points	Sign	Counselling points	Sign
Patient decision aid Shared decision making considering the risks and benefits of anticoagulants. Patient decision aid available ADST (anticoagulation-dst.co.uk)		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	
Explanation of an anticoagulant (increases clotting time and reduces risk of clot formation) and explanation of indication for therapy		• Drug interactions and concomitant medication: avoid NSAID's. Always check with a pharmacist regarding OTC/herbal/complimentary medicines Check dietary intolerance (apixaban and rivaroxaban contain lactose from cow's milk).	
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		Inform all healthcare professionals of DOAC therapy: GP, nurse, dentist, pharmacist i.e., prior to surgery	
Name of drug: generic & brand name		Pregnancy and breastfeeding: potential risk to fetus – obtain medical advice as soon as possible if pregnant/considering pregnancy. Avoid in breastfeeding	
Explanation of dose: strength & frequency		Storage: dabigatran **must** be kept in original packaging – moisture sensitive. All other DOAC are suitable for standard medication compliance aids/ dosette boxes if required	
Duration of therapy: indefinitely for AF		Follow-up appointments, blood tests, and repeat prescriptions: where and when	
To take with food (dabigatran and rivaroxaban). Not required for apixaban or Edoxaban		• Issue relevant patient information AF booklet/leaflet and anticoagulant patient alert card (see patient resources below). Advise always carrying alert card. Signpost to information sources.	
Missed doses: • Edoxaban and rivaroxaban can be taken within 12 hours of missed dose, otherwise omit the missed dose. • Apixaban and dabigatran can be taken within 6 hours of missed dose, otherwise omit the missed dose		Give patient opportunity to ask questions and encourage follow up with community pharmacist (NMS – New Medicine Service)	
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			

APPENDIX 7: Patient information/ Resources

Patient information/ Resources
See the following link for accessing resources for patients on high risk medicines – SPS - Specialist Pharmacy Service – The first stop for professional medicines advice
Atrial Fibrillation Quick Guide for Patients (British Heart Foundation)
NOAC Alert card (explain to patient NOAC/DOAC terms used)  DOAC alert_card.pdf
 Other Information Resources.docx

APPENDIX 8: Management of Dental Patients taking Anticoagulant or Antiplatelet Drugs (Quick Reference Guide)

Quick Reference Guide
See the following link: SDCEP Management of Dental Patients Taking Anticoagulants or Antiplatelet Drugs Quick Reference Guide (2nd Edition)
For full guidance see: www.sdcep.org.uk.

References

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4. https://www.england.nhs.uk/publication/commissioning-recommendations-for-the-national-procurement-of-direct-acting-oral-anticoagulants-doacs
5. Nottingham Area Prescribing Committee Atrial Fibrillation Guidelines- permission obtained for resource use.
6. Derbyshire Medicines Management- Anticoagulation resources – permission obtained
7. Apixaban (Eliquis®): https://www.medicines.org.uk/emc/product/2878/smpc
8. Dabigatran (Pradaxa®) https://www.medicines.org.uk/emc/product/4703/smpc
9. Edoxaban (Lixiana®) - https://www.medicines.org.uk/emc/product/6905/smpc
10. Rivaroxaban (Xarelto®) - https://www.medicines.org.uk/emc/product/2793/smpc
11. NICE CG 196; Atrial fibrillation diagnosis and management 30/6/2021
12. PACEF bulletin Volume 13; No.10, Sept 2019
13. Scottish Dental Clinical Effectiveness Programme- SDCEP Management of Dental Patients Taking Anticoagulants or Antiplatelet Drugs Quick Reference Guide (2nd Edition)
14. British Heart Foundation; AF quick guide
15. Keele University Decision Support ADST (anticoagulation-dst.co.uk)
16. SPS-Specialist Pharmacy Service-Anticoagulant suggestions for adults with swallowing difficulties
17. SPS-Specialist Pharmacy Service-Using oral anticoagulants during breastfeeding
18. Improving the Safe and Effective use of DOACs; NHSE national webinar FAQ section Jan 2023
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28. Managing interactions with direct oral anticoagulants (DOACs) – SPS - Specialist Pharmacy Service – The first stop for professional medicines advice