Anticoagulation for Stroke Prevention in Non-Valvular Atrial Fibrillation: Sheffield joint primary and secondary care guidance

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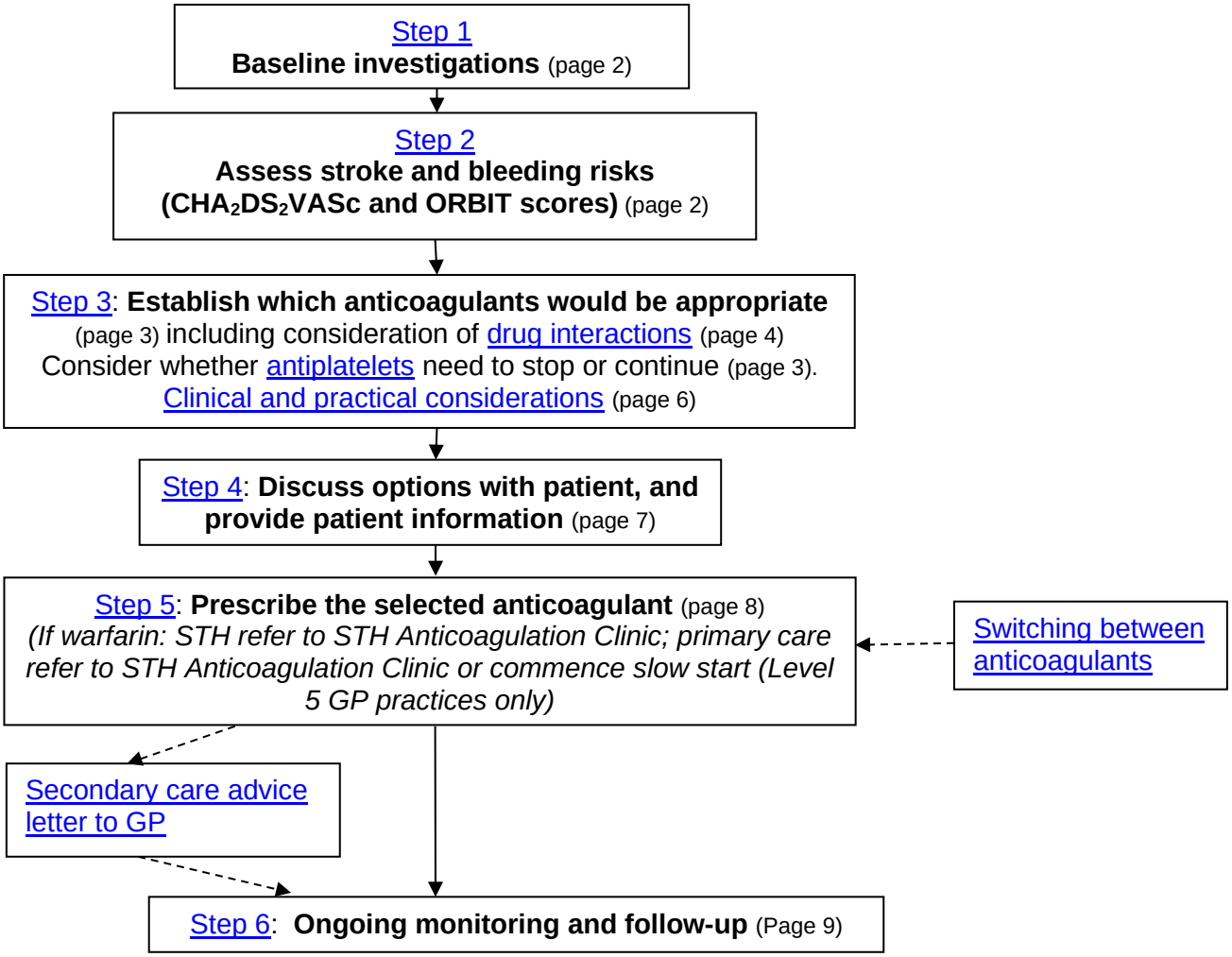
Anticoagulation for Stroke Prevention in Non-Valvular Atrial Fibrillation*:
Sheffield joint primary and secondary care guidance

This document provides guidance to primary and secondary care prescribers in selecting the most suitable anticoagulant for each patient and conducting appropriate baseline and ongoing monitoring.

*** Non-valvular AF is defined as AF in the absence of a mechanical prosthetic heart valve or moderate to severe mitral stenosis (usually of rheumatic origin)**
Patients with aortic valve disease are therefore included in the scope of this guideline.

Do not wait for the results of any echocardiogram that may, or may not, be requested before anticoagulating. Echocardiogram will not affect the decision to anticoagulate.



Additional information:

Key to symbols used throughout this document:
< = less than > = more than CrCl = calculated creatinine clearance DOAC = Direct Oral Anticoagulant
ULN = upper limit of normal

Step 1 - Baseline investigations

● **Blood tests:** U&E, LFT, FBC, clotting screen (results obtained in the previous 6 weeks are acceptable in stable patients. If a patient is being switched to a different anticoagulant, results in the previous 3 months are acceptable; a repeat clotting screen is not required).	● **Height and Weight** (recent i.e. within last 12 months or more recently if suspected weight loss/gain)	● **Blood pressure**	● **Renal function; use calculated creatinine clearance (CrCl) to estimate renal function for DOAC dosing**

Calculated creatinine clearance (Cockroft-Gault):

$$\textbf{Calculated CrCl} = \frac{(140 - \text{age}\ldots\ldots) \times \text{weight (kg)}\ldots\ldots}{\text{Serum Creatinine (micromol/L) .....}} \quad \begin{matrix}\textbf{X 1.04 (female)} \\ \textbf{X 1.23 (male)}\end{matrix} = \ldots\ldots\ldots \text{(mL/min)}$$

For secondary care use ONLY: web-based CrCl calculator, see https://www.mdcalc.com/creatinine-clearance-cockcroft-gault-equation (MDcalc takes no liability for using this tool, use with own clinical judgement).
For Primary care there is a Cockcroft-Gault calculator on the clinical systems. Also see guideline for calculating renal function, which includes guidance on interface issues where the dose of DOAC determined in secondary care may differ from that calculated in primary care.

Step 2 – Assessment of stroke and bleeding risks

Calculate CHA_2DS_2VASc score and stroke risk *Consider anticoagulation in men with a score of 1*
Offer anticoagulation to all patients with score ≥ 2

CHA_2DS_2VASc criteria (treated or untreated conditions)	**Points if present**
Congestive heart failure	1
Hypertension	1
Age 75 years or older	2
Diabetes mellitus	1
Prior **S**troke or TIA	2
Vascular disease	1
Age 65-74 years	1
Sex = female*	1
TOTAL SCORE (max 9)	

CHA_2DS_2VASc score	**Annual stroke risk %**	**5 year risk of thromboembolism %** (hospitalisation or death due to ischaemic stroke, peripheral artery embolism, or pulmonary embolism)
0	0.0	3.45
1	1.3	7.55
2	2.2	15.05
3	3.2	22.05
4	4.0	33.45
5	6.7	52.1
6	9.8	64.25
7	9.6	69.6
8	6.7	70.35
9	15.2	80.4

*Female sex alone does not confer an additional stroke risk, but risk factors present in females confer additional stroke risk compared with males.

Use ORBIT score to identify and assess bleeding risk**

Orbit criteria	**Points if present**
Age >74 years	1
Haemoglobin <13g/dL male or <12g/dL female OR Haematocrit <40% male or <36% female	2
Bleeding history	2
eGFR <60ml/min/1.73m^2	1
Treatment with antiplatelet agents	1
TOTAL SCORE (maximum 7)	

ORBIT score	0-2	3	4-7
Annual bleed risk	Low risk 2.4 bleeds per 100 patient-years	Medium risk 4.7 bleeds per 100 patient-years	High risk 8.1 bleeds per 100 patient–years

see step 3 (next page) for guidance on stopping/continuing antiplatelets with anticoagulation

**ORBIT is recommended by NICE as it has a higher accuracy than other bleeding risk tools
Offer monitoring and support to modify risk factors for bleeding, such as uncontrolled hypertension, concurrent medication, harmful alcohol consumption.

Step 3 – Establish which anticoagulants would be appropriate

Are there any contraindications to anticoagulation? *"recent" = within the previous 2 weeks*

- Confirmed intracranial or intraspinal bleed (usually within last 4 weeks although requires individual assessment)
- Recent trauma or surgery to the head, orbit, or spine
- Recent organ biopsy
- Active bleeding
- Active peptic ulcer, oesophageal varices
- Major bleeding potential or tendency e.g. severe haemophilia
- Uncontrolled hypertension (BP >160/95)
- Infective endocarditis.
- Platelets < 50×10^9/L.
- Chronic liver disease with contraindications to anticoagulation (see page 12)

No

Do any of the following apply?

- Multiple indications for anticoagulation
- Major intraspinal or intracerebral vascular abnormalities
- Recent ischaemic stroke (within 2 weeks)
- Pregnant or breastfeeding.
- Inherited bleeding disorder
- Arteriovenous malformation
- Active malignancy
- Aneurysm
- Proliferative retinopathy (R3)
- CKD5 or haemodialysis or peritoneal dialysis
- Bariatric surgery < 6 months

Yes

Anticoagulation is contra-indicated.
Note that in these circumstances, antiplatelet therapy is generally also unsuitable.
Review at appropriate intervals depending on the contraindication

Yes

Seek specialist advice before starting anticoagulation
(discuss with renal physicians if CKD5/dialysis)

No

Do any of the following apply?

- Mechanical prosthetic heart valve
- Rheumatic mitral stenosis that has not been operated/surgically repaired
- Renal impairment with Creatinine Clearance less than 15mL/min
- **Patient taking drugs which are incompatible with DOACs?** *(see*

Yes

Use warfarin for anticoagulation

No

Is the patient taking any other drugs that may interact with DOACs? (see page 4)

Yes

Eliminate any interacting anticoagulants from the options to be considered

No

The choice of anticoagulant should be made following a discussion between the patient & clinician. NICE guidance recommends a DOAC in preference to warfarin. See NHS England Operational note (16 Jan, updated 6 Sept 2024) for best value DOAC prescribing. The decision should be tailored to the individual patient, taking into account the clinical features and practical considerations outlined on page 6.

Antiplatelets

Stable CHD without previous PCI: stop antiplatelets once patient is anticoagulated (i.e. on DOAC or warfarin with INR >2.0).
If previous PCI, or cardiac infarct <12 months ago: seek advice from supervising cardiologist. If greater than 12 months, continue on oral anticoagulant alone.
Carotid stent or peripheral angioplasty/stent: stop antiplatelets if stenting was >6 weeks ago. Specialists may occasionally recommend longer term antiplatelet therapy to be added to anticoagulation. If in doubt, seek advice from vascular radiologist.
Dual antiplatelet therapy may be continued in addition to anticoagulation in certain circumstances (e.g. low bleed risk, or high stroke risk). This will be a specialist decision and should be clearly documented. *If dual antiplatelet therapy is indicated:* a DOAC should be used in preference to warfarin for anticoagulation.
Existing anticoagulation therapy: Patients with ACS needing an antiplatelet and an anticoagulant should be retained on the DOAC as recommended by the consultant cardiologist and not be switched to an alternative.

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Drug interactions

The information provided below is based on information available at the time of writing and local recommendations. Refer to BNF, SPC and STH Medicines Information/ Sheffield place Medicines Optimisation Team for further information.

	No current data available	✓	Combination appears to be safe	X	Combination has been proven to be clinically unsafe

Caution	Combination is known to / may alter plasma concentration levels. Approach with care and take into account other factors affecting plasma concentration e.g. renal impairment, other concomitant interacting drugs etc. Dose adjustments may be needed.

	Edoxaban	Rivaroxaban	Apixaban	Dabigatran
Azole antifungals:				
Posaconazole	✓	X	X	may increase plasma levels of dabigatran, monitor for signs of bleeding
Voriconazole	✓	X	X	may increase plasma levels of dabigatran, monitor for signs of bleeding
Ketoconazole (oral)	reduce edoxaban dose to 30mg if prescribed concurrently	X	X	X
Fluconazole	✓	✓	✓	may increase plasma levels of dabigatran, monitor for signs of bleeding
Anti-arrhythmics:				
Dronedarone	reduce edoxaban dose to 30mg if prescribed concurrently	X	may increase plasma levels of apixaban. Monitor for signs of bleeding	X
Amiodarone	may increase plasma levels of edoxaban. Monitor for signs of bleeding	may increase plasma levels of rivaroxaban. Monitor for signs of bleeding	may increase plasma levels of apixaban. Monitor for signs of bleeding	may increase plasma levels of dabigatran, adjust dose depending on indication & renal function, monitor for signs of bleeding
Quinidine	may increase plasma levels of edoxaban. Monitor for signs of bleeding	No data currently available	may increase plasma levels of apixaban. Monitor for signs of bleeding	may increase plasma levels of dabigatran, monitor for signs of bleeding. Stop dabigatran if bleeding occurs
Verapamil	may increase plasma levels of edoxaban. Monitor for signs of bleeding	✓	✓	may increase plasma levels of dabigatran (maximum dabigatran dose 110mg BD)
Other drugs:				
Clarithromycin	may increase plasma levels of edoxaban. Monitor for signs of bleeding	may increase plasma levels of rivaroxaban. Monitor for signs of bleeding	may increase plasma levels of apixaban. Monitor for signs of bleeding	may increase plasma levels of dabigatran, monitor for signs of bleeding. Stop dabigatran if bleeding occurs
Erythromycin	reduce edoxaban dose to 30mg during course of erythromycin, if prescribed concurrently. Monitor for signs of bleeding	may increase plasma levels of rivaroxaban	may increase plasma levels of apixaban. Monitor for signs of bleeding	may increase plasma levels of dabigatran, monitor for signs of bleeding. Stop dabigatran if bleeding occurs

Additional notes:

The following drugs are contraindicated with DOACs, and warfarin should be used for anticoagulation:
HIV protease inhibitors
Itraconazole
Rifampicin

The following drugs are either contraindicated or not recommended with apixaban, rivaroxaban and dabigatran. They may reduce the plasma concentrations of edoxaban and should be used with caution on an individual patient basis:
St. John's Wort
Carbamazepine
Phenytoin
Phenobarbital
Primidone

Amiodarone and warfarin
Significant dose adjustments required when amiodarone is started - refer to STH guidelines/ primary care Anticoagulant monitoring service SOP.

Rifampicin and warfarin
Substantial dose adjustments required when rifampicin is started or stopped - refer to STH guidelines / primary care Anticoagulant monitoring SOP

DOACs/Warfarin interact with SSRIs/SNRIs
Increased risk of bleeding when prescribed concurrently, consider the use of PPI.

	Edoxaban	Rivaroxaban	Apixaban	Dabigatran		Additional notes
Ciclosporin	reduce edoxaban dose to 30mg if prescribed concurrently	may increase plasma levels of rivaroxaban. Monitor for signs of bleeding	may increase plasma levels of apixaban. Monitor for signs of bleeding	X		Warfarin has a number of drug/food interactions. Please refer to the BNF, SPC and primary care Anticoagulant monitoring service SOP (Appendix 4) *Seek specialist advice if initiating DOAC in a patient established on tacrolimus.
Tacrolimus*	caution- may increase plasma levels of edoxaban	✓	✓	X		
Ticagrelor (*also note general antiplatelet guidance)*	✓	✓	concurrent prescribing should only be on Cardiologist advice	may increase plasma levels of dabigatran, monitor for signs of bleeding. Stop dabigatran if bleeding occurs		

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Considerations in choosing an anticoagulant
(see pages 3 & 4 before this step)

These are divided into clinical considerations and practical considerations.
The ● symbolises indicate the drug(s) that are more appropriate due to good trial evidence or having a significant amount of experience with their use.

Clinical considerations	Edoxaban	Rivaroxaban	Apixaban	Dabigatran 110mg	Dabigatran 150mg	Warfarin
High risk of bleeding (ORBIT ≥4) ensure modifiable risk factors for bleeding are addressed: blood pressure control, drugs, alcohol			●	●		
History of GI bleed			●	●		●
Risk of dyspepsia or upper GI upset or disorder [1]	●	●	●			●
Low/moderate bleeding risk (ORBIT≤3) and age < 80 years	●	●	●		●	●
High renal clearance - CrCl >95ml/min		●	●			●
Renal impairment – CrCl <15ml/min						●
Body weight <45kg						●
Body weight 45-120kg with a BMI<40kg/m^2	●	●	●			●
Body weight 121-150kg with a BMI<40kgm^2		●	●			●
Body weight >150kg or BMI>40kgm^2						●
Liver impairment – AST/ALT >2 x ULN						●
Practical considerations	**Edoxaban**	**Rivaroxaban**	**Apixaban**	**Dabigatran 110mg**	**Dabigatran 150mg**	**Warfarin**
Once a day formulation preferred	●	●				●
Requirement for a compliance aid [2] (weekly monitored dosage systems filled by pharmacy, or weekly tablet organiser filled by patient, e.g. Nomad, Dossette, etc)	●	●	●			●
Swallowing difficulties or requiring administration through gastric tubes [3]	●	●	●			●
Erratic meal pattern [4]	●		●			●
Concerns with medication adherence / concordance [5]						●
Availability of a reversal agent[6]		●	●	●	●	●

1 - Consider prescribing PPI, but note that PPIs *may* reduce absorption of dabigatran

2 - **Compliance aids: Dabigatran** must be kept in the original packaging with desiccant, therefore is not suitable for use in compliances aids or weekly pill organisers. **Warfarin** may be suitable in a compliance aid following appropriate risk assessment and the existence of a management plan to manage dosage changes. Apixaban, rivaroxaban and edoxaban have no special storage conditions.

3 - Swallowing difficulties and gastric tubes:

- ***Edoxaban, rivaroxaban, and apixaban*** are licensed to be crushed and mixed with water or apple puree immediately prior to oral administration. They may be given through a nasogastric or PEG tube. The tablet should be crushed and administered in a small amount of water via a gastric tube after which it should be flushed with water. None are suitable for administration through feeding tubes which do not terminate in the stomach e.g. NJ, PEJ and PEGJ tubes. If being fed with a bolus PEG/NG feeding regime, rivaroxaban should be administered whilst the feed is in progress.
- ***Warfarin*** 1mg/ml suspension (available from Rosemont) can be used in swallowing difficulties and can be administered through an enteral tube after diluting the suspension with the same volume of distilled water. Crushing warfarin tablets is off-licence.
- ***Dabigatran*** must be administered in its original form. The capsules must not be opened or chewed/crushed.

4 - DOACs currently have no known food or alcohol interactions. Rivaroxaban **must** be taken with food.

5 - Patients with poor concordance may be at a 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.

6- At the time of writing, licensed commercially available reversal agents are available for dabigatran, apixaban & rivaroxaban. Vitamin K will fully reverse anticoagulation with warfarin but *will not* reverse the DOACs.

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Step 4 – Discuss options with patient, and provide patient information

For patients who lack capacity, a decision should be taken in the patients "best interests" in line with GMC guidance.

The discussion should cover:

- Stroke and bleeding risk
- Suitable anticoagulation options and the differences between them
    - Dosing
    - Monitoring
    - The effects of other medications, food and alcohol
- How to use anticoagulants
    - The correct dose
    - What to do in case of a missed dose
- Duration of anticoagulation treatment
- Possible side effects and what to do if these occur

Provide written information covering:

- How anticoagulation may affect dental treatment
- How anticoagulants may affect activities such as sports and travel
- When and how to seek medical help
- Women of childbearing potential who are taking anticoagulants should be advised to take contraceptive precautions and contact their GP urgently if they think they may be pregnant.
- Rivaroxaban must be taken with food to ensure full absorption
- Dabigatran should be taken with food to reduce the likelihood of heartburn/indigestion

Patient information and resources:

Drug information booklets:

- Apixaban – (generic and brand Eliquis®) PIL and alert cards can be downloaded and printed from the eMC; see Patient Information (PIL) and Risk materials tabs respectively.

- Rivaroxaban – (generic and brand Xarelto®) PIL and alert cards can be downloaded and printed from the eMC; see Patient Information (PIL) and Risk materials tabs respectively.

- Edoxaban – Lixiana® PIL and alert cards can be downloaded and printed from the links or ordered from Daiichi Sankyo UK (telephone 0800 198 5000).

- Dabigatran – Pradaxa® PIL and alert card can be downloaded and printed from the links. Copies of the patient booklet can be ordered by HCP only from distribution.bra@boehringer-ingelheim.com

- A warfarin anticoagulant record (yellow book) can be ordered via NHS Forms or Primary Care Support England (PCSE)

- A generic DOAC information booklet can be ordered via NHS Forms or Primary Care Support England (PCSE)

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Step 5 – Prescribe the selected anticoagulant

Apixaban generic – joint best value overall and best value twice daily DOAC*	
5mg twice a day (usual dose)	**2.5mg twice a day** Reduced dose if: ● CrCl 15-29ml/min **OR** If **two** of the following apply: ● Age ≥ 80 yrs ● Body weight ≤ 60kg ● serum creatinine >133 micromol/L

Rivaroxaban generic – joint best value overall and best value once daily DOAC*	
20mg once a day (usual dose)	**15mg once a day** Reduced dose if CrCl 15-49ml/min

Edoxaban	
60mg once a day (usual dose)	**30mg once a day** Reduced dose if one or more of the following apply: ● CrCl 15-50ml/min ● Body weight ≤ 60kg ● Concomitant use of the following P-glycoprotein (P-gp) inhibitors: ciclosporin, dronedarone, erythromycin, or ketoconazole *From trial data, a trend towards decreasing efficacy with increasing creatinine clearance was observed for edoxaban compared with well-managed warfarin. Therefore, edoxaban should only be used in patients with a high creatinine clearance (>95ml/min) after a careful evaluation of the individual thromboembolic and bleeding risk.*

Dabigatran	
150mg twice a day (usual dose)	**110mg twice a day** Reduced dose if any of the following apply: • Age ≥80 years • Concomitant verapamil Reduced dose should be considered in the following, based on individual assessment of thromboembolic risk and risk of bleeding: • Patients between 75-80 years • Patients with moderate renal impairment (CrCl 30-50ml/min) • Patients with gastritis, esophagitis or gastroesophageal reflux • Other patients at increased risk of bleeding (e.g., ORBIT >3, history of GI bleed, etc.). **Note that dabigatran is not licensed with CrCl <30ml/min**

***NHS England Operational note** (16 Jan, updated 6 Sept 2024). Clinicians should use the best value DOAC that is clinically appropriate for the patient.

Warfarin	
Primary care • If the practice is contracted to provide Level 5 anticoagulation, *and* the patient is suitable, start Slow Start warfarin. • Otherwise, refer to STH Anticoagulation Clinic for warfarin initiation. The referral letter/form must be signed by a prescriber, and needs to include: ○ Indication for anticoagulation ○ Target INR range (generally 2.0 – 3.0 for stroke prevention in AF) ○ Duration of anticoagulation (generally long term for AF) ○ A full list of current medication ○ Instructions regarding whether antiplatelets are to stop or continue once INR is >2.0 (see page 3 for guidance)	**Secondary care** Start warfarin following the warfarin loading protocol on the STH Warfarin Prescription and Monitoring Chart. On discharge from hospital, refer patient to STH Anticoagulation Clinic via ICE.
The Anticoagulation Clinic will provide the patient with an initial supply of warfarin 1mg and 3mg tablets, and GPs will be required to add warfarin on to the repeat prescription thereafter. In certain circumstances it may be appropriate to only prescribe the 1mg tablets (e.g., patients on daily doses of less than 3mg, visual impairment, or lack of confidence handling a combination of strengths).	

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Step 6 - Ongoing monitoring of anticoagulation

<table>
<tr><th></th><th colspan="4">All DOACs</th><th>Warfarin</th></tr>
<tr><td>Early monitoring until patient stabilised</td><td colspan="4">Monitoring/follow-up to be undertaken by GP.
No routine anticoagulation monitoring is needed.
Ideally assess patient after 1 month initially and at least every 3 months thereafter to:
Assess compliance and reinforce advice regarding regular dosing schedule.
Enquire about adverse effects such as bleeding.
Assess for the presence of thromboembolic events.
Enquire about other medicines, including OTC medicines.</td><td>INR monitoring as per STH Anticoagulation Clinic guidelines or Sheffield primary care anticoagulation SOP.
After 6 months
Review anticoagulation control (see below for unstable criteria)</td></tr>
<tr><td>Long term monitoring

National guidance as per NICE CKS and SPS

Blue font- Alternative local guidance for a pragmatic approach if above not suitable for patient and/or practice.</td><td colspan="4">• U&E, LFT and FBC at least annually.
• More frequent U&Es, LFTs and FBCs advised if declining renal function (calculated CrCl <60ml/min) see below, frail or increasing age >75, intercurrent illness that may impact on renal or liver function.</td><td rowspan="2">Annually
LFTs
U&E
FBC
Review anticoagulation control (see below for unstable criteria)</td></tr>
<tr><td>Edoxaban
U&E:
CrCl >60ml/min – annually
CrCl<60ml/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.
OR
U&E:
CrCl >60ml/min – annually
CrCl 36 – 60ml/min – every 6 months
CrCl 15 – 35ml/min – every 3 months
CrCl <15ml/min- do not use</td><td>Rivaroxaban
U&E:
CrCl >60ml/min – annually
CrCl<60ml/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.
OR
U&E:
CrCl >60ml/min – annually
CrCl 36 – 60ml/min – every 6 months
CrCl 15 – 35ml/min – every 3 months
CrCl <15ml/min- do not use</td><td>Apixaban
U&E:
CrCl >60ml/min – annually
CrCl<60ml/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.
OR
U&E:
CrCl >60ml/min – annually
CrCl 36 – 60ml/min – every 6 months
CrCl 15 – 35ml/min – every 3 months
CrCl <15ml/min- do not use</td><td>Dabigatran
U&E:
Patient <75 years and CrCl >60ml/min – annually
Age >75 years or fragile – every 6 month
CrCl 30 - 60ml/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.
OR
U&E:
Patient <75 years and CrCl >60ml/min – annually
Age >75 years or fragile – every 6 months
CrCl 36 – 60ml/min – every 6 months
CrCl 30 – 35ml/min – every 3 months
CrCl <30ml/min – do not use</td></tr>
</table>

	All DOACs				Warfarin
Action required if abnormal results	**Edoxaban** ***Renal function:*** • If CrCl 15-50ml/min, reduce dose of edoxaban to 30mg OD • If CrCl <15ml/min, stop edoxaban and switch to warfarin. ***Liver function:*** Elevated liver enzymes (ALT/AST >2 x ULN) or total bilirubin ≥1.5 x ULN: stop edoxaban & switch to warfarin (also see page 12). ***Full blood count:*** An unexplained fall in haemoglobin and/or haematocrit may suggest that occult bleeding is occurring and may require further investigations.	**Rivaroxaban** ***Renal function:*** • If CrCl 15-49ml/min, reduce dose of rivaroxaban to 15mg OD • If CrCl <15ml/min, stop rivaroxaban and switch to warfarin. ***Liver function:*** Elevated liver enzymes (ALT/AST >2 x ULN), or Child-Pugh score B or C: stop rivaroxaban & switch to warfarin (also see page 12). ***Full blood count:*** An unexplained fall in haemoglobin and/or haematocrit may suggest that occult bleeding is occurring and may require further investigations.	**Apixaban** ***Renal function:*** • Reduce dose to 2.5mg BD if indicated by combination of age, weight and serum creatinine • Reduce dose to 2.5mg BD if CrCl 15-29ml/min • If CrCl <15ml/min, stop apixaban and switch to warfarin. ***Liver function:*** Elevated liver enzymes (ALT/AST >2 x ULN) or total bilirubin ≥1.5 x ULN: stop apixaban & switch to warfarin (also see page 12). ***Full blood count:*** An unexplained fall in haemoglobin and/or haematocrit may suggest that occult bleeding is occurring and may require further investigations.	**Dabigatran** ***Renal function:*** • If CrCl 30-50ml/min, reduce dose of dabigatran to 110mg BD • If CrCl <30ml/min, stop dabigatran and switch to warfarin. ***Liver function:*** Elevated liver enzymes (ALT/AST >2 x ULN): stop dabigatran & switch to warfarin (also see page 12). ***Full blood count:*** An unexplained fall in haemoglobin and/or haematocrit may suggest that occult bleeding is occurring and may require further investigations.	**Unstable anticoagulation:** Review adherence to medication. Review diet, alcohol intake and other lifestyle factors. Switch to DOAC if appropriate (see considerations). ***UNSTABLE ANTICOAGULATION – criteria*** *Any one of:* • *2 INRs >5 in the last 6 months* • *1 INR >8 in the last 6 months* • *2 INRs <1.5 in the last 6 months (outwith planned interruptions)* • *Time in therapeutic range <65%*

Switching between anticoagulants

Warfarin to DOAC	DOACs to warfarin
	INRs taken during the switch must be taken using venous samples. The results of Coaguchek® and other point-of-care INR testing will be erroneously affected by the presence of DOAC. **Refer patient to STH Anticoagulation Clinic to initiate warfarin**
The SmPCs for individual DOACs recommend different INR thresholds for starting DOACs after stopping warfarin. The EHRA 2021 gives pragmatic guidance and recommends that the INR should be <2.5 when the DOAC is started. • If INR <2 commence DOAC the same day • If INR between 2 and 2.5 commence DOAC the next day ideally (or the same day) • If INR between 2.5 and 3 withhold warfarin for 24-72 hours, re-check INR and then initiate DOAC	**Edoxaban to warfarin** • Start warfarin following an approved loading protocol (NB Slow Start is not suitable). • Patients taking a 60mg dose of edoxaban should be switched to 30mg. Patients taking a 30mg dose should be switched to 15mg. • INR must be taken using a venous sample, at least 24 hours after the last dose of edoxaban (and immediately prior to the next dose of edoxaban). Continue edoxaban until INR ≥ 2.0
	Rivaroxaban to warfarin • Start warfarin following an approved loading protocol (NB Slow Start is not suitable). • Continue taking rivaroxaban. • INR must be taken using a venous sample, at least 24 hours after the last dose of rivaroxaban (and immediately prior to the next dose of rivaroxaban). • Continue rivaroxaban until INR ≥ 2.0
	Dabigatran to warfarin* • Start warfarin following an approved loading protocol (NB Slow Start is not suitable). • Continue taking dabigatran. • INR must be taken using a venous sample, at least 12 hours after the last dose of dabigatran (and immediately prior to the next dose of dabigatran). • Continue dabigatran until INR ≥ 2.0 • INRs checked whilst on dabigatran or within 3 days of stopping dabigatran must be taken using a venous sample. The result should be interpreted with caution as dabigatran can increase INR. ***The above advice is derived from pragmatic interpretation of information presented in the SPC for dabigatran.
	Apixaban to warfarin • Start warfarin following an approved loading protocol (NB Slow Start is not suitable). • Continue taking apixaban. • INR must be taken using a venous sample, at least 12 hours after the last dose of apixaban (and immediately prior to the next dose of apixaban). • Continue apixaban until INR ≥ 2.0

DOAC to DOAC
Start new drug when dose of previous drug would have been due. Patients must not be on more than one DOAC at once.

Parenteral anticoagulant (e.g. dalteparin, fondaparinux) to DOAC DOAC to parenteral anticoagulant
Start new drug when dose of previous drug would have been due. Patients must not be on more than one anticoagulant at once. **For management during surgical procedures, see STH guideline "Bridging anticoagulation: the peri-procedural management of patients on oral anticoagulants (excluding neurosurgery)"**

Parenteral anticoagulant to warfarin
Follow STH warfarin guidelines. NB: This would not normally be done in primary care.

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Dental procedures and other surgery

Dental Procedures

Please refer to the Management of Dental Patients Taking Anticoagulants or Antiplatelet Drugs, which has been published by the Scottish Dental Clinical Effectiveness Programme (SDCEP). The British Dental Association (BDA) advises that it is intended for use throughout the UK and aims to provide clear and practical advice for the dental team, including on assessment of bleeding risk and decision making for treatment planning.
In addition to the full guidance, resources include a quick reference guide and a range of patient leaflets.

- Full guidance and Quick Reference Guide
- Patient information leaflet: Anticoagulant or Antiplatelet Medication and Your Dental Treatment
- Patient information leaflet: Post-Treatment Advice for Dental Patients
- Pre-treatment instructions: Direct Oral Anti-Coagulants
- Pre-treatment instructions: Warfarin

Non-dental procedures

For non-dental procedures, see STH guideline "Bridging anticoagulation: the peri-procedural management of patients on oral anticoagulants (excluding neurosurgery)"

Anticoagulation for AF in patients with chronic liver disease

The following guidance has been produced by the hepatology team for the benefit of non-specialists.

1 - Is there evidence of current liver decompensation?

- bilirubin >40 micromol/L
- albumin <35 g/L
- prolonged PT **or** APTT

If any of these features are present, seek specialist advice before commencing anticoagulation

↓

If none of the above are present, proceed to question 2

↓

2 - Is there evidence of cirrhosis?

- liver biopsy
- present or previous ascites
- present or previous varices (on endoscopy **or** imaging)
- persistently low platelet count
- irregular liver edge or splenomegaly on ultrasound
- Fibro scan (transient elastography) score of >15 KPa *(recommended in NAFLD patients with fibrosis risk in intermediate or high range **or** in other cases where there is doubt)*

If any of these features are present, need to exclude oesophago-gastric varices or other bleeding sources by gastroscopy before considering anticoagulation

↓

If none of the above are present – can cautiously commence warfarin anticoagulation for AF.
Seek specialist advice before commencing DOACs (edoxaban, apixaban, rivaroxaban or dabigatran)

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