January 2022: Note that NICE NG196 AF: diagnosis and management, has been updated since this guidance was endorsed and now recommends a DOAC as the first line anticoagulant for stroke prevention in AF. Consult the NICE guidance for further information. This guidance will be reviewed in due course.

NHS Barnsley Hospital NHS Foundation Trust | NHS South West Yorkshire Partnership NHS Foundation Trust | NHS Barnsley Clinical Commissioning Group

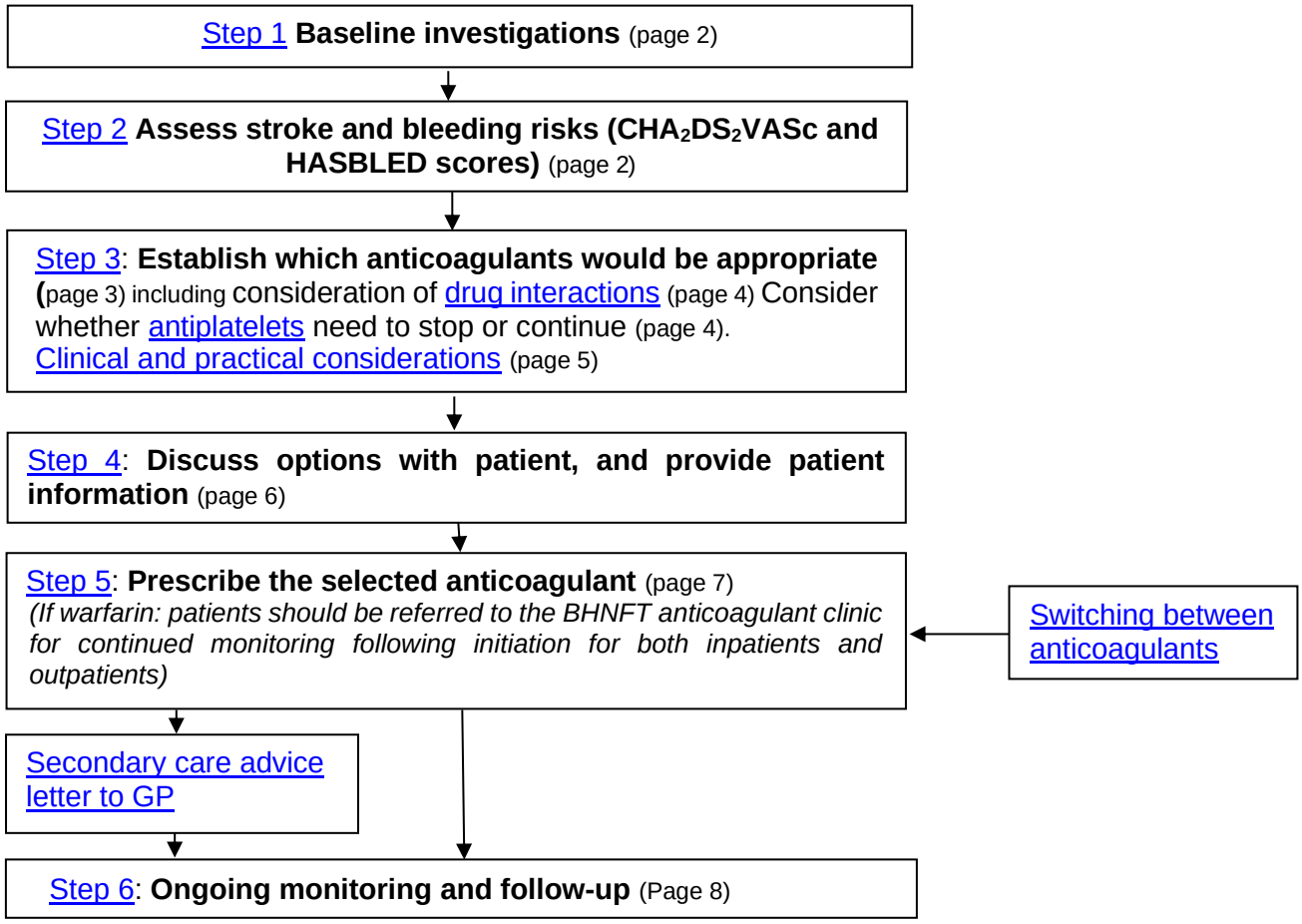
Anticoagulation for Stroke Prevention in Non-Valvular Atrial Fibrillation*: Joint primary and secondary care guidance

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. *This document has been reproduced and adapted from the Sheffield Teaching Hospitals/NHS Sheffield joint anticoagulation for stroke prevention in NVAF guidance version 2.*

*** 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, mitral regurgitation in any degree and bioprosthetic valves are therefore included in the scope of this guideline

Confirm the diagnosis of AF. Evidence of AF should be confirmed with a surface ECG, monitoring interpreted by a trained medical professional, monitoring device (i.e. 24 hr ECG monitor) or pacemaker. Blood pressure devices or clinical findings of an irregular heartbeat should only prompt further investigations but they are not sufficient to establish the diagnosis.

Do not wait for the results of any echocardiogram that may, or may not, be requested before anticoagulation. The 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.)	● **Height and Weight** (recent i.e. within last 12 months or more recently if suspected weight loss/gain)	● **Blood pressure**	● **Renal function using calculated creatinine clearance (CrCl).** Do not use eGFR.

Calculated creatinine clearance (Cockroft-Gault):

Calculated CrCl= $\frac{(140 - \text{age}\ldots\ldots) \times \text{weight (kg)}\ldots\ldots}{\text{Serum Creatinine (micromol/L) .....}}$ **X 1.04 (female)** **X 1.23 (male)** = ...(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.

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**
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 to males.

Use HASBLED to identify and treat modifiable bleeding risk factors

Note that many stroke risk factors are also bleeding risk factors. Bleeding risk should not be used as an excuse not to anticoagulate, but the HASBLED score should be used to identify risk factors that can be modified (e.g. treat hypertension, review drugs that increase bleeding risk, educate patients about alcohol intake).

HASBLED criteria (conditions that are being successfully treated do not count towards the score)	**Points**
Hypertension (most recent systolic blood pressure >160 mm Hg)	**1**
Abnormal renal* and liver† function (1 point each) * chronic dialysis, renal transplantation, or serum creatinine ≥200 micromol/L. † chronic hepatic disease (e.g. cirrhosis) or biochemical evidence of significant hepatic derangement (bilirubin 2 to 3 times the upper limit of normal, in association with AST / ALT / Alk Phos 3 x ULN, etc)	**1 or 2**
Stroke (not TIA)	**1**
Bleeding tendency/predisposition [History of bleeding or predisposition (anaemia)]	**1**
Labile INRs (if on warfarin) [i.e.2 INRs >5 or 1 INR >8 within the last 6 months, 2 INRs <1.5 within the last 6 months (outwith planned interruptions), time in therapeutic range <65%]	**1**
Elderly (age >65 years)	**1**
Drugs or alcohol (1 point each) Concomitant antiplatelets** or nonsteroidal anti-inflammatory drugs, or alcohol intake >8 units/week	**1 or 2**
TOTAL SCORE (maximum 9)	

HASBLED score	0	1	2	3	4	≥5
Annual bleed risk %	1.13	1.02	1.88	3.74	8.7	12.5

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

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 11)

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

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

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
- Extreme of body weights <50 kg, >120 kg or BMI 40.
- **Patient taking drugs which are incompatible with DOACs?** e.g.
  - HIV protease inhibitors
  - Carbamazepine
  - Itraconazole
  - Rifampicin
  - Phenytoin
  - Primidone
  - St John's Wort
  - Phenobarbital

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

The choice of anticoagulant should be made following a discussion between the patient and clinician.
The decision should be tailored to the individual patient, taking into account the clinical features and practical considerations outlined on page 5.

Antiplatelets

****As per NICE guidelines antiplatelets do not hold license for stroke prevention in AF.**
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 on double or triple therapy. Refer to separate guidance for the combined use of anticoagulant and antiplatelet therapy.

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Drug interactions

The information provided below is based on information available at the time of writing. Refer to BNF, SPC and STH Medicines Information/CCG Medicines Management Team for further information.

	No current data available	✓	Combination has been proven 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.

	Apixaban	Rivaroxaban	Dabigatran	Edoxaban
Azole antifungals:				
Posaconazole	X	X	caution - may increase plasma levels of dabigatran	reduce edoxaban dose by 50%
Voriconazole	X	X	X	
Fluconazole		✓		
Ketoconazole	X	X	X	reduce edoxaban dose by 50%
Anti-arrhythmics:				
Dronedarone	caution - may increase plasma levels of apixaban	X	X	reduce edoxaban dose by 50%
Amiodarone			caution - may increase plasma levels of dabigatran	caution- may increase plasma levels of edoxaban
Quinidine			caution - may increase plasma levels of dabigatran	caution - may increase plasma levels of edoxaban
Verapamil			caution - may increase plasma levels of dabigatran (maximum dabigatran dose 110mg BD)	caution- may increase plasma levels of edoxaban
Other drugs:				
Clarithromycin/ Erythromycin		✓	caution - may increase plasma levels of dabigatran	reduce edoxaban dose by 50%
Tacrolimus	X	X	X	caution- may increase plasma levels of edoxaban
Ciclosporin	X	X	X	Caution-may increase plasma levels of edoxaban
Ticagrelor *also note general antiplatelet guidance*			caution - may increase plasma levels of dabigatran	

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 contraindicated 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

Amiodarone and warfarin
Significant dose adjustments required when amiodarone is started – advise close monitoring of INR.

Rifampicin and warfarin
Substantial dose adjustments required when rifampicin is started or stopped – advise close monitoring of INR.

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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	Apixaban	Rivaroxaban	Dabigatran 110mg	Dabigatran 150mg	Edoxaban	Warfarin
Liver impairment – AST/ALT >2 x ULN						●
History of GI bleed			●			●
Risk of dyspepsia or upper GI upset or disorder [1]	●	●			●	●
Extremes of body weight (less than 50kg or greater than 120kg)[2]						●
Low bleeding risk (HAS-BLED≤3) and age < 80 years				●		
High risk of bleeding (HAS-BLED≥3 after attempts to adjust for modifiable risk factors (blood pressure control, drugs and alcohol)	●		●			
Practical considerations	**Apixaban**	**Rivaroxaban**	**Dabigatran 110mg**	**Dabigatran 150mg**	**Edoxaban**	**Warfarin**
Once a day formulation preferred		●			●	●
Requirement for a compliance aid [3] (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[4]	●	●			●	●
Erratic meal pattern [5]	●				●	●
Concerns with medication adherence / concordance [6]						●
Availability of a direct reversal agent[7]	●	●	●	●		●

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

2 – **Extremes of body weight:** Limited data is available on the use of DOACs in patients weighing less than 50kg or more than 120kg and there may be a risk of over or under-anticoagulation respectively. . Warfarin treatment may be preferable in such patients since anticoagulation can be monitored using INR. Use of DOACs in these patient groups should be based on discussion with the patient taking into account individual bleeding risk and other patient specific factors. Where uncertainty remains, individual patients may be discussed with the relevant specialists.

3 - **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.

4 - Swallowing difficulties and gastric tubes:

- ***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. Neither rivaroxaban nor apixaban 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 (licensed product 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.
- ***Edoxaban*** is not licensed for crushing at the time of writing, although data is available to support its use.

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

6 - 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.

7 - Vitamin K will fully reverse anticoagulation with warfarin but *will not* reverse the DOACs. At the time of writing, licensed commercially available reversal agents are available for dabigatran (reversal agent = Praxbind®) and rivaroxaban and apixaban (Ondexxya®). Further information can be found in the BHNFT guideline for the management of bleeding induced by DOACs.

Patients with renal impairment requiring anticoagulant therapy

CrCl (ml/min)	>80	50-79	30-49	15-29	<15
Dabigatran	150mg BD	110mg BD		Contraindicated	
Rivaroxaban	20 mg OD		15 mg OD		Not recommended
Apixaban	5 mg BD Reduce dose to 2.5 mg BD if <u>two</u> of the following apply: • Age ≥80 years • Weight ≤60 kg • Serum creatinine ≥133 µmol/l			2.5 mg BD	Not recommended
Edoxaban	60 mg OD Reduce dose to 30 mg OD if ≥1 of: • Weight ≤60 Kg • Concomitant use of P-gp inhibitors.		30 mg OD		Not recommended
Warfarin	Dose as per INR. Close INR monitoring may be warranted in patients with unstable renal function or severe impairment.				

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 resources:
NICE AF patient decision aid summarises information on the things people with atrial fibrillation most often want to think about and discuss with their healthcare team when deciding on which anticoagulant treatment option to take. The person making this decision can then weigh up the possible advantages and disadvantages of the different treatment options.

Drug information booklets:

- Warfarin – NPSA "yellow book"
- Apixaban – Eliquis®
    - Booklets and patient alert cards can be ordered from Bristol-Myers Squibb Medical Information (telephone: 0800 731 1736; e-mail: medical.information@bms.com)
- Rivaroxaban – Xarelto®
    - Booklets and alert cards can be downloaded and printed from http://www.xarelto-info.co.uk/hcp/
- Dabigatran – Pradaxa® patient information packs (leaflet and alert card) can be ordered from https://www.pradaxa.co.uk/
- Edoxaban- Lixiana® booklets and patient alert cards can be downloaded and printed from http://www.lixiana.co.uk/en-gb/hcp-resources/patient-support-materials

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Step 5 – Prescribe the selected anticoagulant

The list is in no particular order, there is no preference between DOACS and the decision should be considered according to patients characteristics and choice

Warfarin	
Primary care • If the practice is contracted to provide Level 5 anticoagulation, *and* the patient is suitable use the Warfarin "Slow Start" Regimen. *Anticoagulation Guidance: Standard Operating Procedure for the provision of a Level 3, 4 and 5 Anticoagulation Service ; Appendix 5 (A copy can be obtained from the Medicines Management Team and will be made available on the BEST website in due course).*	**Secondary care** Start warfarin following the warfarin loading protocol on the BHNFT Warfarin prescription and monitoring chart. On discharge from hospital, this prescription chart doubles as the referral form for follow up and should be sent to BHNFT Anticoagulation Clinic. Patients initiated on warfarin via outpatient clinics can be referred to the clinic using the AF referral form.
The Anticoagulation Clinic will provide the patient with an initial supply of warfarin 0.5mg, 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).	

Rivaroxaban	
20mg once a day (usual dose)	**15mg once a day** Reduced dose if CrCl 15-49ml/min (or in combination with antiplatelet drugs – see separate guideline)

Apixaban	
****Please note that recent audits have shown significant amount of patients being prescribed a lower dose than recommended which leads to inappropriate stroke prevention with similar bleeding risk. Consider carefully the next instructions.**	
5mg twice a day (usual dose)	**2.5 mg twice a day if:** • CrCl 15-29ml/min **OR** Reduced dose if **two** of the following apply: ● Age ≥ 80 yrs ● Body weight ≤ 60kg ● serum creatinine >133 micromol/L

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. HASBLED ≥3, history of GI bleed, etc). **Note that dabigatran is not licensed with CrCl <30ml/min**

Edoxaban	
60mg once a day (usual dose)	**30mg once a day** Reduced dose if any 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 after a careful evaluation of the individual thromboembolic and bleeding risk.*

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 every 3 months 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 BHNFT Anticoagulation Clinic guidelines
After 6 months
Review anticoagulation control (see below for unstable criteria)</td></tr>
<tr><td colspan="6">For all forms of anticoagulation please consider performing an early FBC within 2-6 weeks to confirm stable haemoglobin levels.</td></tr>
<tr><td>Long term monitoring</td><td colspan="4">3 monthly follow-up/assessment as above.
U&E, LFT and FBC at least annually.
More frequent U&Es / LFTs advised if intercurrent illness that may impact on renal or liver function.
If calculated CrCl <60ml/min, or patient >75yrs on dabigatran, monitor U&E more frequently as below:</td><td rowspan="2">Annually
LFTs
U&E
FBC
Review anticoagulation control (see below for unstable criteria)</td></tr>
<tr><td></td><td>Apixaban</td><td>Rivaroxaban</td><td>Edoxaban</td><td>Dabigatran</td></tr>
<tr><td>Action required if abnormal results</td><td>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
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.</td><td>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
Renal function:
If CrCl 15-49ml/min, reduce dose of rivaroxaban to 15mg OD
If CrCl <15ml/min, stop rivaroxaban and switch to warfarin.</td><td>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
Renal function:
If CrCl 15-50ml/min, reduce dose of edoxaban to 30mg OD
If CrCl <15ml/min, stop edoxaban and switch to warfarin.</td><td>U&E:
Patient <75 years and CrCl >60ml/min – annually
CrCl 36 – 60ml/min – every 6 months
CrCl 30 – 35ml/min – every 3 months
CrCl <30ml/min – do not use
Age >75 years or fragile – every 6 mth
Renal function:
If CrCl 30-50ml/min, reduce dose of dabigatran to 110mg BD
If CrCl <30ml/min, stop dabigatran and switch to warfarin.</td><td>Unstable anticoagulation:
Review adherence to medication.
Review diet, alcohol intake and other lifestyle factors.
Switch to DOAC if appropriate (see considerations).</td></tr>
</table>

	All DOACs				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 11) ***Full blood count:*** An unexplained fall in haemoglobin and/or haematocrit may suggest that occult bleeding is occurring and may require further investigations.	***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 11). ***Full blood count:*** An unexplained fall in haemoglobin and/or haematocrit may suggest that occult bleeding is occurring and may require further investigations	***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 11) ***Full blood count:*** An unexplained fall in haemoglobin and/or haematocrit may suggest that occult bleeding is occurring and may require further investigations	***Liver function:*** Elevated liver enzymes (ALT/AST >2 x ULN): stop dabigatran & switch to warfarin (also see page 11). ***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 – 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

Consider changing from warfarin to DOAC in suitable cases with unstable INR (<65% of time in therapeutic range).

From	To	How to Switch?
DOAC	DOAC	• Initiate when next dose is due except where higher plasma concentrations expected (e.g. renal impairment).
DOACs to Vitamin K Antagonists (VKA) 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.		
Apixaban	Vitamin K Antagonist (VKA)	• Start VKA (NB slow loading not approriate) and continue Apixaban for at least 2 days. After 2 days of co-administration an INR should be obtained before the next scheduled dose of Apixaban. • Co-administration should be continued until the INR is ≥2.0.
Rivaroxaban		• Rivaroxaban = Start VKA and continue Rivaroxaban until the INR is ≥2.0. While patients are on both Rivaroxaban and VKA the INR should not be tested earlier than 24 hours after the previous dose but prior to the next dose of Rivaroxaban.
Dabigatran		• VKA should be started according to renal function. If: ○ CrCL ≥ 50 mL/min, VKA should be started 3 days before discontinuing Dabigatran ○ CrCL ≥ 30 - <50 mL/min, VKA should be started 2 days before discontinuing Dabigatran
Edoxaban		• Edoxaban = See SPC via this link.
Vitamin K Antagonist (VKA)	Apixaban	• Stop VKA and commence Apixaban once INR is <2.0.
	Rivaroxaban	• Rivaroxaban = Stop VKA and commence Rivaroxaban once: ○ INR is ≤3.0 if for prevention of stroke and systemic embolism. ○ INR is ≤2.5 if for DVT, PE and prevention of recurrence.
	Dabigatran	• Stop VKA and commence Dabigtran once INR is <2.0.
	Edoxaban	• Stop VKA and start Edoxaban once INR is ≤2.5.

• **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 drug at once. **For management during surgical procedures, see BHNFT bridging guideline version 2.2.**

Parenteral anticoagulant to warfarin
Advise 2 consecutive INRs >2 before stopping parenteral anticoagulant, unless INR increases above target range NB: This would not normally be done in primary care.

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Dental procedures and other surgery

Warfarin

Procedures which may be performed on warfarin with INR <4.0 will be advised by the dentist.
In patients who are stably anticoagulated on warfarin, an INR check 72 hours prior to the procedure is recommended. This allows sufficient time for dose modification if necessary to ensure a safe INR on the day of the procedure.

Non-invasive dental procedures (as advised by the dentist).
No INR check required.

Apixaban, rivaroxaban, dabigatran or edoxaban

Dental procedures including minor oral surgery or up to 3 dental extractions, prosthodontics, conservation, endodontics, hygiene phase therapy and orthodontics: **Omit the dose taken in the morning of the procedure and restart after the procedure (as advised by the dentist), provided there are no concerns about bleeding.**

Non-dental procedures

For non-dental procedures, see BHNFT Bridging guideline version 2.2.

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

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

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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

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

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This version of the guideline was reproduced and adapted from the Sheffield Teaching Hospitals/NHS Sheffield joint guidleine on Anticoagulation for prevention of NVAF (v2.0, 2018) by Dr Erin Leal (Staff Grade Cardiology Dr BHNFT) and Gillian Turrell (Lead Pharmacist, Medicines Information and Cardiology, BHNFT). This guideline has been subject to consultation and endorsement by the Area Prescribing Committee on 12th August 2020.