

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

## Version 2 June 2018

Approved by STH MMTC: July 2018

NHS Sheffield APG: August 2018

Review date: August 2020

## Version 2.1 August 2020

**Review date extended to: August 2023**

**Approved by: FSG under delegated authority of APG      Date: August 2020**

The review date on these guidelines has been extended by the AF Special Interest Group June 2020. The group concluded that the guidelines remain valid but additional consideration must be given by prescribers to the latest anticoagulation guidance issued to safely manage patients on anticoagulation during the COVID-19 pandemic and whilst social distancing remains in place.

### **Latest anticoagulation guidance during COVID-19:**

For the latest anticoagulation guidance during COVID-19 see national guidance [here](#) produced by NHS England and NHS Improvement. This includes guidance for those patients shielding and those unsuitable to switch to DOACs.

There is also local guidance to safely switch warfarin patients to DOACs [here](#).

One option for warfarin patients unsuitable to switch to DOACs is Self-testing of INR; for local guidance see [here](#).

All these guidelines are available on the Sheffield CCG Intranet [COVID-19](#) page.

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June 2020

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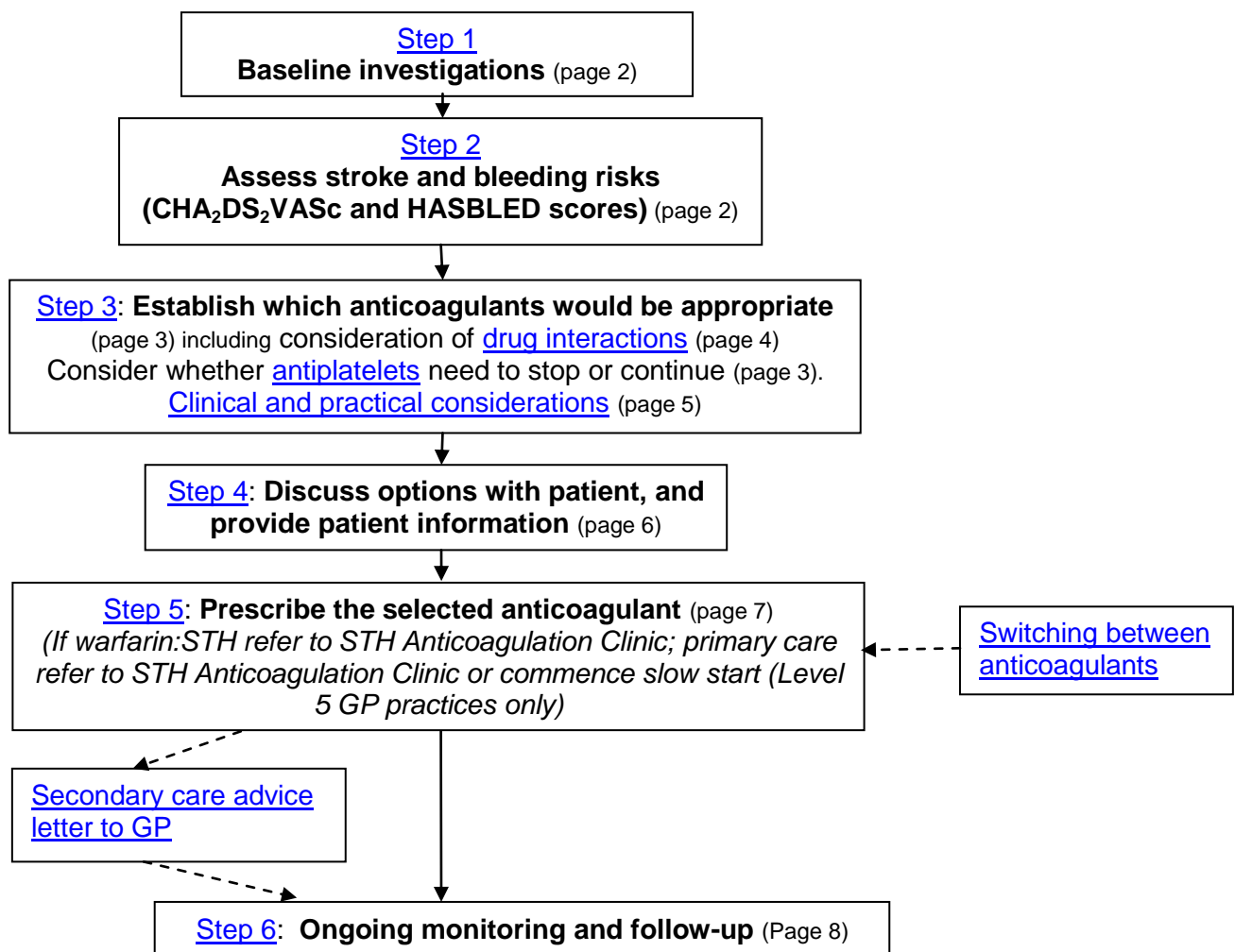
## Anticoagulation for Stroke Prevention in Non-Valvular Atrial Fibrillation\*: Joint primary and secondary care guidance

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.

**\* 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:

[Switching between anticoagulants](#) – page 10

[Dental procedures and other surgery](#) - page 11

[Anticoagulation for AF in patients with chronic liver disease](#) – page 11

### Key to symbols used throughout this document:

< = less than > = more than CrCl = calculated creatinine clearance  
ULN = upper limit of normal

DOAC = Direct Oral Anticoagulant

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Approved by STH MMTC: July 2018

NHS Sheffield APG: August 2018 / August 2020

Review date: August 2020 extended August 2023

## Step 1 - Baseline investigations

<ul style="list-style-type: none"> <li><b>Blood tests:</b> U&amp;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.)</li> </ul>	<ul style="list-style-type: none"> <li><b>Height and Weight</b> (recent i.e. within last 12 months or more recently if suspected weight loss/gain)</li> </ul>	<ul style="list-style-type: none"> <li><b>Blood pressure</b></li> </ul>	<ul style="list-style-type: none"> <li><b>Renal function using calculated creatinine clearance (CrCl).</b> Do not use eGFR.</li> </ul>
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Calculated creatinine clearance (Cockcroft-Gault):

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

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: [http://www.intranet.sheffieldccg.nhs.uk/Downloads/Medicines%20Management/prescribing%20guidelines/supplement\\_for\\_SPAF\\_guidelines.pdf](http://www.intranet.sheffieldccg.nhs.uk/Downloads/Medicines%20Management/prescribing%20guidelines/supplement_for_SPAF_guidelines.pdf)

## Step 2 – Assessment of stroke and bleeding risks

**Calculate CHA<sub>2</sub>DS<sub>2</sub>VASc score and stroke risk** *Consider anticoagulation in men with a score of 1*  
*Offer anticoagulation to all patients with score ≥ 2*

CHA <sub>2</sub> DS <sub>2</sub> VASc criteria (treated or untreated conditions)	Points
Congestive heart failure	1
Hypertension	1
Age 75 years or older	2
Diabetes mellitus	1
Prior Stroke or TIA	2
Vascular disease	1
Age 65-74 years	1
Sex = female*	1
<b>TOTAL SCORE (max 9)</b>	

CHA <sub>2</sub> DS <sub>2</sub> VASc 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**

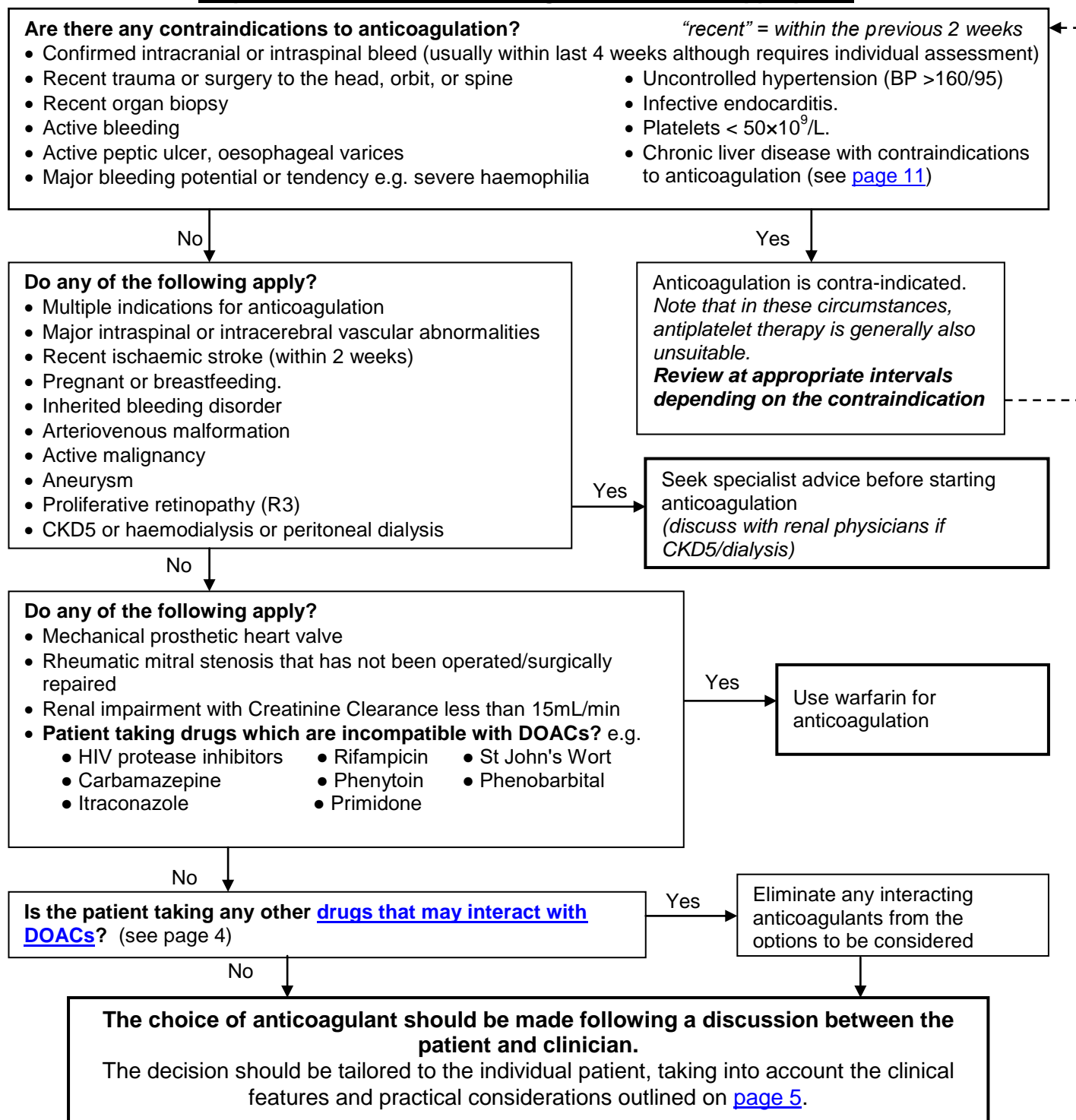
Note that many stroke risk factors are also bleeding risk factors. Bleeding risk should not be used as an excuse not to anticoagulate, but the HASBLED score should be used to identify risk factors that can be modified (e.g. treat hypertension, review drugs that increase bleeding risk, educate patients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

HASBLED criteria (conditions that are being successfully treated do not count towards the score)	Points
<b>Hypertension</b> (most recent systolic blood pressure >160 mm Hg)	<b>1</b>
<b>Abnormal renal* and liver† function (1 point each)</b> * 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)	<b>1 or 2</b>
<b>Stroke</b> (not TIA)	<b>1</b>
<b>Bleeding tendency/predisposition</b> [History of bleeding or predisposition (anaemia)]	<b>1</b>
<b>Labile INRs (if on warfarin)</b> [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%]	<b>1</b>
<b>Elderly</b> (age >65 years)	<b>1</b>
<b>Drugs or alcohol (1 point each)</b> Concomitant antiplatelets** or nonsteroidal anti-inflammatory drugs, or alcohol intake >8 units/week	<b>1 or 2</b>
<b>TOTAL SCORE (maximum 9)</b>	

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



#### 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

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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
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<b>Caution</b>	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.
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	Apixaban	Rivaroxaban	Dabigatran	Edoxaban
<b>Azole antifungals:</b>				
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%
<b>Anti-arrhythmics:</b>				
Dronedaron	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
<b>Other drugs:</b>				
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
<b>Ticagrelor</b> <i>also note general antiplatelet guidance</i>			caution - may increase plasma levels of dabigatran	

<u>Additional notes:</u>
<p><b>The following drugs are contraindicated with DOACs, and warfarin should be used for anticoagulation:</b>                      HIV protease inhibitors                      Itraconazole                      Rifampicin</p> <p><b>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:</b>                      St. John's Wort                      Carbamazepine                      Phenytoin                      Phenobarbital</p> <p><b>Amiodarone and warfarin</b>                      Significant dose adjustments required when amiodarone is started - refer to STH guidelines/CCG anticoagulant monitoring SOP</p> <p><b>Rifampicin and warfarin</b>                      Substantial dose adjustments required when rifampicin is started or stopped - refer to STH guidelines / CCG anticoagulant monitoring SOP</p>

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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
High risk of bleeding (HAS-BLED $\geq$ 3 after attempts to adjust for modifiable risk factors (blood pressure control, drugs and alcohol))	●		●			
History of GI bleed	●		●			●
Risk of dyspepsia or upper GI upset or disorder <sup>1</sup>	●	●			●	●
Low bleeding risk (HAS-BLED $\leq$ 3) and age < 80 years				●		
Renal impairment – CrCl <15ml/min						●
Extremes of body weight (less than 45kg or greater than 130kg)						●
Liver impairment – AST/ALT >2 x ULN						●
Practical considerations	Apixaban	Rivaroxaban	Dabigatran 110mg	Dabigatran 150mg	Edoxaban	Warfarin
Once a day formulation preferred		●			●	●
Requirement for a compliance aid <sup>2</sup> (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 <sup>3</sup>	●	●			●	●
Erratic meal pattern <sup>4</sup>	●				●	●
Concerns with medication adherence / concordance <sup>5</sup>						●
Availability of a reversal agent <sup>6</sup>			●	●		●

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:

- **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.

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, a licensed commercially available reversal agent, Praxbind® is available for dabigatran. Vitamin K will fully reverse anticoagulation with warfarin but *will not* reverse the DOACs.



## **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](mailto: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

Warfarin	
<p><b>Primary care</b></p> <ul style="list-style-type: none"> <li>• If the practice is contracted to provide Level 5 anticoagulation, <i>and</i> the patient is suitable, start Slow Start warfarin.</li> <li>• Otherwise, refer to STH Anticoagulation Clinic for warfarin initiation. The referral letter/form must be signed by a prescriber, and needs to include:               <ul style="list-style-type: none"> <li>○ Indication for anticoagulation</li> <li>○ Target INR range (generally 2.0 – 3.0 for stroke prevention in AF)</li> <li>○ Duration of anticoagulation (generally long term for AF)</li> <li>○ Full list of current medication</li> <li>○ Give instructions regarding whether antiplatelets are to stop or continue once INR is &gt;2.0 (see <a href="#">page 3</a> for guidance)</li> </ul> </li> </ul>	<p><b>Secondary care</b></p> <p>Start warfarin following the warfarin loading protocol on the <a href="#">STH Warfarin Prescription and Monitoring Chart</a>.</p> <p>On discharge from hospital, refer patient to STH Anticoagulation Clinic using <a href="#">Anticoagulation Referral Form A</a>.</p>
<p>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).</p>	

Apixaban	
<p><b>5mg twice a day</b> (usual dose)</p>	<p><b>2.5mg twice a day if:</b></p> <ul style="list-style-type: none"> <li>• CrCl 15-29ml/min</li> </ul> <p><b>OR</b></p> <p>Reduced dose if <b>two</b> of the following apply:</p> <ul style="list-style-type: none"> <li>• Age ≥ 80 yrs</li> <li>• Body weight ≤ 60kg</li> <li>• serum creatinine &gt;133 micromol/L</li> </ul>

Rivaroxaban	
<p><b>20mg once a day</b> (usual dose)</p>	<p><b>15mg once a day</b> Reduced dose if CrCl 15-49ml/min</p>

Dabigatran	
<p><b>150mg twice a day</b> (usual dose)</p>	<p><b>110mg twice a day</b> Reduced dose if any of the following apply:</p> <ul style="list-style-type: none"> <li>• Age ≥80 years</li> <li>• Concomitant verapamil</li> </ul> <p>Reduced dose should be considered in the following, based on individual assessment of thromboembolic risk and risk of bleeding:</p> <ul style="list-style-type: none"> <li>• Patients between 75-80 years</li> <li>• Patients with moderate renal impairment (CrCl 30-50ml/min)</li> <li>• Patients with gastritis, esophagitis or gastroesophageal reflux</li> <li>• Other patients at increased risk of bleeding (e.g. HASBLED ≥3, history of GI bleed, etc).</li> </ul> <p><b>Note that dabigatran is not licensed with CrCl &lt;30ml/min</b></p>

Edoxaban	
<p><b>60mg once a day</b> (usual dose)</p>	<p><b>30mg once a day</b> Reduced dose if any of the following apply:</p> <ul style="list-style-type: none"> <li>• CrCl 15-50ml/min</li> <li>• Body weight ≤ 60kg</li> <li>• Concomitant use of the following P-glycoprotein (P-gp) inhibitors: ciclosporin, dronedarone, erythromycin, or ketoconazole</li> </ul> <p><i>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.</i></p>

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### Step 6 - Ongoing monitoring of anticoagulation

	<b>All DOACs</b>				<b>Warfarin</b>
<b>Early monitoring until patient stabilised</b>	Monitoring/follow-up to be undertaken by GP. <ul style="list-style-type: none"> <li>No routine anticoagulation monitoring is needed</li> <li>Ideally assess patient every 3 months to:                             <ul style="list-style-type: none"> <li>Assess compliance and reinforce advice regarding regular dosing schedule.</li> <li>Enquire about adverse effects such as bleeding.</li> <li>Assess for the presence of thromboembolic events</li> <li>Enquire about other medicines, including OTC medicines</li> </ul> </li> </ul>				INR monitoring as per STH Anticoagulation Clinic guidelines or <a href="#">Sheffield primary care anticoagulation SOP</a> . <b>After 6 months</b> Review anticoagulation control (see below for unstable criteria)
<b>Long term monitoring</b>	<ul style="list-style-type: none"> <li>3 monthly follow-up/assessment as above.</li> <li>U&amp;E, LFT and FBC at least annually.</li> <li>More frequent U&amp;Es / LFTs advised if intercurrent illness that may impact on renal or liver function.</li> <li>If calculated CrCl &lt;60ml/min, or patient &gt;75yrs on dabigatran, monitor U&amp;E more frequently as below:</li> </ul>				<b>Annually</b> <ul style="list-style-type: none"> <li>LFTs</li> <li>U&amp;E</li> <li>FBC</li> <li>Review anticoagulation control (see below for unstable criteria)</li> </ul>
	<b>Apixaban</b>	<b>Rivaroxaban</b>	<b>Edoxaban</b>	<b>Dabigatran</b>	
	<b>U&amp;E:</b> <ul style="list-style-type: none"> <li>CrCl &gt;60ml/min – annually</li> <li>CrCl 36 – 60ml/min – every 6 months</li> <li>CrCl 15 – 35ml/min – every 3 months</li> <li>CrCl &lt;15ml/min – do not use</li> </ul>	<b>U&amp;E:</b> <ul style="list-style-type: none"> <li>CrCl &gt;60ml/min – annually</li> <li>CrCl 36 – 60ml/min – every 6 months</li> <li>CrCl 15 – 35ml/min – every 3 months</li> <li>CrCl &lt;15ml/min – do not use</li> </ul>	<b>U&amp;E:</b> <ul style="list-style-type: none"> <li>CrCl &gt;60ml/min – annually</li> <li>CrCl 36 – 60ml/min – every 6 months</li> <li>CrCl 15 – 35ml/min – every 3 months</li> <li>CrCl &lt;15ml/min – do not use</li> </ul>	<b>U&amp;E:</b> <ul style="list-style-type: none"> <li>Patient &lt;75 years and CrCl &gt;60ml/min – annually</li> <li>CrCl 36 – 60ml/min – every 6 months</li> <li>CrCl 30 – 35ml/min – every 3 months</li> <li>CrCl &lt;30ml/min – do not use</li> <li>Age &gt;75 years or fragile – every 6 mth</li> </ul>	
<b>Action required if abnormal results</b>	<b>Renal function:</b> <ul style="list-style-type: none"> <li>Reduce dose to 2.5mg BD if indicated by combination of age, weight and serum creatinine</li> <li>Reduce dose to 2.5mg BD if CrCl 15-29ml/min</li> <li>If CrCl &lt;15ml/min, stop apixaban and switch to warfarin.</li> </ul>	<b>Renal function:</b> <ul style="list-style-type: none"> <li>If CrCl 15-49ml/min, reduce dose of rivaroxaban to 15mg OD</li> <li>If CrCl &lt;15ml/min, stop rivaroxaban and switch to warfarin.</li> </ul>	<b>Renal function:</b> <ul style="list-style-type: none"> <li>If CrCl 15-50ml/min, reduce dose of edoxaban to 30mg OD</li> <li>If CrCl &lt;15ml/min, stop edoxaban and switch to warfarin.</li> </ul>	<b>Renal function:</b> <ul style="list-style-type: none"> <li>If CrCl 30-50ml/min, reduce dose of dabigatran to 110mg BD</li> <li>If CrCl &lt;30ml/min, stop dabigatran and switch to warfarin.</li> </ul>	<b>Unstable anticoagulation:</b> Review adherence to medication. Review diet, alcohol intake and other lifestyle factors. Switch to DOAC if appropriate (see <a href="#">considerations</a> ).

All DOACs				Warfarin	
	<p><b>Liver function:</b> Elevated liver enzymes (ALT/AST &gt;2 x ULN) or total bilirubin <math>\geq</math>1.5 x ULN: stop apixaban &amp; switch to warfarin (also see <a href="#">page 11</a>)</p> <p><b>Full blood count:</b> An unexplained fall in haemoglobin and/or haematocrit may suggest that occult bleeding is occurring and may require further investigations.</p>	<p><b>Liver function:</b> Elevated liver enzymes (ALT/AST &gt;2 x ULN), or Child-Pugh score B or C: stop rivaroxaban &amp; switch to warfarin (also see <a href="#">page 11</a>).</p> <p><b>Full blood count:</b> An unexplained fall in haemoglobin and/or haematocrit may suggest that occult bleeding is occurring and may require further investigations</p>	<p><b>Liver function:</b> Elevated liver enzymes (ALT/AST &gt;2 x ULN) or total bilirubin <math>\geq</math>1.5 x ULN: stop edoxaban &amp; switch to warfarin (also see <a href="#">page 11</a>)</p> <p><b>Full blood count:</b> An unexplained fall in haemoglobin and/or haematocrit may suggest that occult bleeding is occurring and may require further investigations</p>	<p><b>Liver function:</b> Elevated liver enzymes (ALT/AST &gt;2 x ULN): stop dabigatran &amp; switch to warfarin (also see <a href="#">page 11</a>).</p> <p><b>Full blood count:</b> An unexplained fall in haemoglobin and/or haematocrit may suggest that occult bleeding is occurring and may require further investigations.</p>	<p><b>UNSTABLE ANTICOAGULATION – criteria</b> Any one of:</p> <ul style="list-style-type: none"> <li>• 2 INRs &gt;5 in the last 6 months</li> <li>• 1 INR &gt;8 in the last 6 months</li> <li>• 2 INRs &lt;1.5 in the last 6 months (outwith planned interruptions)</li> <li>• Time in therapeutic range &lt;65%</li> </ul>

### Switching between anticoagulants

Warfarin to DOAC	DOACs to warfarin
<p><b>Warfarin to apixaban</b></p> <ul style="list-style-type: none"> <li>• Stop warfarin.</li> <li>• Start apixaban when INR &lt;2.0</li> </ul>	<p>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.</p> <p><b>Refer patient to STH Anticoagulation Clinic to initiate warfarin</b></p> <p><b>Apixaban to warfarin</b></p> <ul style="list-style-type: none"> <li>• Start warfarin following an approved loading protocol (NB Slow Start is not suitable).</li> <li>• Continue taking apixaban.</li> <li>• 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).</li> <li>• Continue apixaban until INR ≥ 2.0</li> </ul>
<p><b>Warfarin to rivaroxaban</b></p> <ul style="list-style-type: none"> <li>• Stop warfarin.</li> <li>• Start rivaroxaban when INR &lt;3.0</li> </ul>	<p><b>Rivaroxaban to warfarin</b></p> <ul style="list-style-type: none"> <li>• Start warfarin following an approved loading protocol (NB Slow Start is not suitable).</li> <li>• Continue taking rivaroxaban.</li> <li>• 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).</li> <li>• Continue rivaroxaban until INR ≥ 2.0</li> </ul>
<p><b>Warfarin to dabigatran</b></p> <ul style="list-style-type: none"> <li>• Stop warfarin.</li> <li>• Start dabigatran when INR &lt;2.0</li> </ul>	<p><b>Dabigatran to warfarin*</b></p> <ul style="list-style-type: none"> <li>• Start warfarin following an approved loading protocol (NB Slow Start is not suitable).</li> <li>• Continue taking dabigatran.</li> <li>• 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).</li> <li>• Continue dabigatran until INR ≥ 2.0</li> <li>• 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.</li> </ul> <p>*The above advice is derived from pragmatic interpretation of information presented in the SPC for dabigatran.</p>
<p><b>Warfarin to edoxaban</b></p> <ul style="list-style-type: none"> <li>• Stop warfarin.</li> <li>• Start edoxaban when INR ≤ 2.5</li> </ul>	<p><b>Edoxaban to warfarin</b></p> <ul style="list-style-type: none"> <li>• Start warfarin following an approved loading protocol (NB Slow Start is not suitable).</li> <li>• Patients taking a 60mg dose of edoxaban should be switched to 30mg. Patients taking a 30mg dose should be switched to 15mg.</li> <li>• 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).</li> <li>• Continue edoxaban until INR ≥ 2.0</li> </ul>

#### DOAC to DOAC

**Start new drug when dose of previous drug would have been due.**

Patients must not be on more than one drug 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 drug 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

### 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 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 (apixaban, rivaroxaban, dabigatran or edoxaban)**

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## **Version history**

Version 2 is adapted from version 1 developed by Rebecca Hammond, Anticoagulant Pharmacist, STH and V-Lin Cheong, Medicines Management Pharmacist, Sheffield CCG on behalf of AF interest group. Date published May 2015

Version 2.1: see [cover sheet](#) for details