Guidelines for oral anticoagulation of patients with non-valvular atrial fibrillation (AF) to prevent stroke in adults

Contents

1. Atrial Fibrillation Anticoagulant Clinical Decision Aid - Overview and checklist for initiation 2
2. Assessment of stroke and bleeding risks for patients with non-valvular AF 3
3. Prescriber decision support for anticoagulating patients with non-valvular AF 4
4. Choice of oral anticoagulant based on patient characteristics 5
5. Choice of NOAC based on patient characteristics 7
6. Choice of NOAC based on patient logistical considerations 8
7. NOAC dosing for stroke risk reduction in non-valvular AF 9
   Calculating renal function – Cockroft and Gault formula 10
8. NOAC monitoring and follow-up 11
9. Warfarin monitoring and follow-up 12
10. Communication across secondary/primary care interface - Information to be transferred to GPs 13

Appendix 1: NOAC patient counselling checklist 14
Appendix 2: Switching between oral anticoagulants for non-valvular atrial fibrillation 15
Appendix 3: Comparative costs of NOACs 17

Acknowledgments 18
References 19
1. Atrial Fibrillation Anticoagulant Clinical Decision Aid - Overview and checklist for initiation

1.1. Patient details and risk assessments

<table>
<thead>
<tr>
<th>Date</th>
<th>NHS number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient Name</td>
<td></td>
</tr>
<tr>
<td>DOB</td>
<td>Age</td>
</tr>
<tr>
<td>CHA₂DS₂Vasc Score</td>
<td>HAS-BLED Score</td>
</tr>
<tr>
<td>Annual Stroke Risk</td>
<td>Annual Bleed Risk</td>
</tr>
<tr>
<td>Modifiable Risk Factors</td>
<td></td>
</tr>
<tr>
<td>Contra-indications to anticoagulation</td>
<td></td>
</tr>
</tbody>
</table>

1.2. Baseline clinical screening checklist

<table>
<thead>
<tr>
<th>U&amp;Es (Creatinine)</th>
<th>Weight* (kg)</th>
<th>FBC</th>
<th>LFTs</th>
<th>Baseline Clotting</th>
<th>BP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline (All patients)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Recent weight, ideally at time of clinical screening

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

1.3. Choice of anticoagulant

**Warfarin [ ]** non-vitamin K oral anticoagulant (NOAC)** [ ]** referral [ ]

**Choice of NOAC**

**Interactions with patients current medicines**

**NOAC Dose**

**Patient Counselling**

See page 7-8

Drug interactions with NOACs

See page 9

See appendix 1: NOAC counselling checklist

1.4. Ongoing Monitoring required

<table>
<thead>
<tr>
<th>NOAC</th>
<th>U&amp;Es (Creatinine), Weight (kg)*, FBC, LFTs, BP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Warfarin</td>
<td></td>
</tr>
</tbody>
</table>

*Recent weight, ideally at time of clinical screening
2. Assessment of stroke and bleeding risks for patients with non-valvular AF

Online calculators are available on GP clinical systems

- CHA2DS2-VASc scoring system for risk of stroke
- HASBLED scoring system for risk of bleed

### CHA2DS2Vasc Scoring System for AF Stroke Risk\(^{1,2,3}\)

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Congestive heart failure/LV dysfunction</td>
<td>1</td>
</tr>
<tr>
<td>Hypertension</td>
<td>1</td>
</tr>
<tr>
<td>Age ≥ 75</td>
<td>2</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>1</td>
</tr>
<tr>
<td>Stroke/TIA/systemic arterial embolism</td>
<td>2</td>
</tr>
<tr>
<td>Vascular disease (previous MI, peripheral arterial disease, aortic plaque)</td>
<td>1</td>
</tr>
<tr>
<td>Age 65 -74</td>
<td>1</td>
</tr>
<tr>
<td>Sex (male 0, female 1)</td>
<td>F 1</td>
</tr>
</tbody>
</table>

**Total score (maximum score 9)**

### HAS BLED scoring for Bleeding Risk\(^{1,2,3}\)

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension (uncontrolled, &gt; 160mmHg systolic)</td>
<td>1</td>
</tr>
<tr>
<td>Chronic liver disease or Bilirubin 2xULN with AST/ALT/ALP 3xULN</td>
<td>1</td>
</tr>
<tr>
<td>Abnormal renal function (creatinine ≥200micromol/L, renal transplant or chronic dialysis)</td>
<td>1</td>
</tr>
<tr>
<td>Stroke</td>
<td>1</td>
</tr>
<tr>
<td>History of major bleeding* or predisposition</td>
<td>1</td>
</tr>
<tr>
<td>Labile INRs, time in range less than 60%</td>
<td>1</td>
</tr>
<tr>
<td>Elderly (age ≥ 65 or frail condition)</td>
<td>1</td>
</tr>
<tr>
<td>Drugs (e.g. concomitant antiplatelet, NSAIDs) or alcohol (≥8 drinks/week) (1 point each)</td>
<td>1 or 2</td>
</tr>
</tbody>
</table>

**Total score (maximum score 9)**

\(^*\) Bleeding requiring hospitalisation and/or causing decrease in haemoglobin > 20g/L and/or requiring ≥ 2 units of blood

### Interpreting CHA\(_2\)DS\(_2\)Vasc and HASBLED Score

<table>
<thead>
<tr>
<th>CHA(_2)DS(_2) Vasc</th>
<th>Events per 100 patients/year</th>
<th>HAS BLED Score</th>
<th>Major bleeding events per 100 patients/year in anticoagulation users</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Stroke/TIA/peripheral emboli</td>
<td>Ischaemic stroke</td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>0.3</td>
<td>0.2</td>
<td>0</td>
</tr>
<tr>
<td>1</td>
<td>1.0</td>
<td>0.6</td>
<td>1</td>
</tr>
<tr>
<td>2</td>
<td>3.3</td>
<td>2.5</td>
<td>2</td>
</tr>
<tr>
<td>3</td>
<td>5.3</td>
<td>3.7</td>
<td>3</td>
</tr>
<tr>
<td>4</td>
<td>7.8</td>
<td>5.5</td>
<td>4</td>
</tr>
<tr>
<td>5</td>
<td>11.7</td>
<td>8.4</td>
<td>5</td>
</tr>
<tr>
<td>6</td>
<td>15.9</td>
<td>11.4</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>18.4</td>
<td>13.1</td>
<td></td>
</tr>
</tbody>
</table>
3. Prescriber decision support for anticoagulating patients with non-valvular AF

For most people benefit of anticoagulation outweighs bleeding risk. Discuss in conjunction with patient information leaflet: Patient information leaflet: AF and treatment options to reduce stroke risk

For people with increased bleeding risk (e.g. HASBLED ≥3), address modifiable risk factors:
- Uncontrolled hypertension
- Concurrent medication (e.g. aspirin, NSAID)
- Harmful alcohol consumption
- Poorly controlled (labile) INRs

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

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

Contraindications to anticoagulation

The following list of contraindications are taken from individual Summary of Product Characteristics (SPC’s)\(^4\)\(^-\)\(^7\), MHRA safety updates 2009\(^8\) and 2013\(^9\) and NICE CKS\(^10\). Discuss the clinical management plan with a Haematologist if there is a known contraindication to anticoagulant treatment. The list below is not exhaustive; see individual SPCs for additional contraindications for individual anticoagulants (https://www.medicines.org.uk/emc)

- Clinically significant bleeding
- Recent intracranial haemorrhage
- A significant risk of major bleeding such as:
  - Current or recent upper gastrointestinal ulceration
  - Presence of malignant neoplasm at high risk of bleeding
  - Known or suspected oesophageal varices
  - Recent brain, head or spinal injury/surgery or ophthalmic surgery
  - Arteriovenous malformation, vascular aneurysm or major intraspinal or intracerebral vascular abnormalities
  - Within 72 hours of major surgery
- Concomitant treatment with any other anticoagulant

4. Choice of oral anticoagulant based on patient characteristics

NICE CG 180 states: “Anticoagulation may be with vitamin K antagonist (warfarin) or non-vitamin K antagonist oral anticoagulants (apixaban, dabigatran etexilate, rivaroxaban)”. Subsequent to this, NICE TA355 recommended edoxaban as a treatment option for non valvular AF.

NB: Patients should already have been screened for an absolute contraindication to oral anticoagulation as per guidance on page 4.

- Does patient have a mechanical heart valve or moderate to severe mitral stenosis?
  - Yes: Warfarin
  - No: Does the patient have a contra-indication to a NOAC? (4,5,6,7,16)

- Does the patient have a contra-indication to a NOAC? (4,5,6,7,16)
  - Yes: Warfarin (or LMWH in pregnancy)
  - No: - CrCl less than 15ml/minute
    - Known hypersensitivity
    - Pregnancy (any stage)
    - Hepatic disease associated with coagulopathy
    - Contraindicated concomitant drugs (See common drug interactions with NOACs)
    - See individual SPC’s for a complete list of contraindications (https://www.medicines.org.uk/emc)

- Does the patient have a CrCl less than 30ml/minute?
  - Yes: Consider warfarin
  - No: Does the patient weigh more than 120kg or have a BMI greater than 40kg/m²?

- Does the patient weigh more than 120kg or have a BMI greater than 40kg/m²?
  - Yes: Recommend warfarin**
  - No: Patients with a CrCl < 30ml/min were excluded from clinical trials (CrCl 25ml/min for apixaban). (12-15) ESC guidance 2018 suggests that warfarin should be preferred in these patients. (16)

- Limited data on NOACs in extreme obesity, available pharmacodynamics and pharmacokinetic data suggests potential for underdosing. International Society of Thrombosis and Haemostasis recommend warfarin. (16,17)

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

Yes

Consider seeking advice from Haematology

Patients with ALT/AST 2x ULN (ALT 3x ULN for rivaroxaban) or bilirubin ≥ 1.5ULN were excluded from landmark NOAC trials. All NOACs are contra-indicated in patients with hepatic disease associated with coagulopathy and clinically relevant bleeding risk.4,7,16

Has the patient been diagnosed with antiphospholipid syndrome?

Yes

Warfarin or refer to Haematology

NOACs are not recommended in patients with antiphospholipid syndrome, particularly high-risk patients (those who test positive for all 3 antiphospholipid tests - lupus anticoagulant, anti-cardiolipin antibodies, and anti-beta 2 glycoprotein I antibodies), as they could be associated with increased rates of recurrent thrombotic events compared with therapy with a vitamin K antagonist.18

Patient history of non-compliance or are they likely to miss doses?

Yes

Consider warfarin

The protective effect of NOACs on the risk of stroke may fade 12 - 24 hours after a dose is taken.4,5,6,7 Warfarin allows monitoring of effectiveness if non-compliance is anticipated.

Does the patient have an indication for combined antiplatelet therapy?

Yes

For example: History of vascular stenting, acute coronary syndrome +/- percutaneous coronary intervention (PCI), elective PCI

Discuss management plan with cardiologists/specialists

Is there a reason a NOAC therapy may be advantageous? Does the patient have a contra-indication or adverse drug reaction to warfarin? Patient preference for NOAC therapy?

Yes

For example: Poor compliance with INR monitoring or variable dosing, variable intake of medicines that interact with warfarin, need for monitored dosage system, patients poorly controlled on warfarin: TTR < 65% in the past 6 months or 2x INR > 5 or 1x INR > 8, 2 x INRs < 1.5 despite good compliance1

See NOAC decision algorithm (page 7)
5. Choice of NOAC based on patient characteristics

NB: There have been no head-to-head trials between NOACs. The guidance below is based on indirect comparisons. Dosing advice can be found on page 9.

If there are no specific clinical considerations, use the NOAC of lowest acquisition cost

Are there any specific clinical considerations?

- Recurrent stroke/TIA despite well controlled warfarin
  - Dabigatran 150mg
    - Low-dose dabigatran 110mg BD is the only NOAC to demonstrate a clinical and statistically significant reduction in ischaemic stroke when compared to warfarin.\(^{12}\)
  - Edoxaban
  - Apixaban
    - Subgroup analysis of ARISTOTLE trial (apixaban) suggests that the greatest reduction of major haemorrhage compared to warfarin was in patients with a CrCl < 50ml/min.\(^{19}\)
    - The ENGAGE trial demonstrated that edoxaban has a similar efficacy to other factor Xa inhibitors but with a more favourable bleeding profile in patients with renal impairment.\(^{19,20}\)

- High risk of major bleeding (HAS-BLED≥3)
  - Dabigatran 150mg
  - Apixaban
  - Subgroup analysis of ARISTOTLE trial (apixaban) suggests that the greatest reduction of major haemorrhage compared to warfarin was in patients with a CrCl < 50ml/min.\(^{19}\)
  - The ENGAGE trial demonstrated that edoxaban has a similar efficacy to other factor Xa inhibitors but with a more favourable bleeding profile in patients with renal impairment.\(^{19,20}\)

- History of gastrointestinal (GI) bleeding or ulcer
  - Dabigatran 150mg
    - Dabigatran 150mg, edoxaban 60mg and rivaroxaban were shown to have higher GI bleeding risk than warfarin in clinical trials.\(^{12,13,15}\)
    - Apixaban and dabigatran 110mg had similar risks to warfarin.\(^{12,14}\)
    - Dabigatran is associated with higher rates of dyspepsia than warfarin, due to acidic coating of the capsule.\(^{12}\)
  - Apixaban
  - Edoxaban
  - Rivaroxaban

- GI symptoms or dyspepsia
  - Edoxaban
  - Apixaban

- Preference for once daily dosing
  - Edoxaban
  - Rivaroxaban

- Renal impairment CrCl 30 - 49ml/min
  - Edoxaban
  - Apixaban
### 6. Choice of NOAC based on patient logistical considerations

<table>
<thead>
<tr>
<th>Are there any specific logistical considerations?</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Need for a monitored dosage system?</strong></td>
</tr>
<tr>
<td><strong>Swallowing difficulties or administration of medicines via enteral tube?</strong></td>
</tr>
</tbody>
</table>
7. NOAC dosing for stroke risk reduction in non-valvular AF

- NB: The dose guidance below is specific to the use of NOAC therapy for stroke risk reduction in AF. Dosing recommendations for deep vein thrombosis, pulmonary embolism, acute coronary syndrome or post-hip/knee replacement can be found in the individual Summary of Product Characteristics via https://www.medicines.org.uk/emc
- Always check the latest Summary of Product Characteristics https://www.medicines.org.uk/emc for dosage adjustments (e.g. in liver impairment) and drug interactions before prescribing.
- See page 10 for calculating creatinine clearance using the Cockcroft-Gault equation for NOAC dose calculation.
- In general, as there is insufficient evidence for efficacy at lower doses for some agents, doses of NOACs should not be reduced unless a dose reduction is clinically indicated as outlined in the table below.

<table>
<thead>
<tr>
<th>Dabigatran⁴</th>
<th>Rivaroxaban⁵</th>
<th>Apixaban⁶</th>
<th>Edoxaban⁷</th>
</tr>
</thead>
<tbody>
<tr>
<td>Standard dose:</td>
<td>Standard dose:</td>
<td>Standard dose:</td>
<td>Standard dose:</td>
</tr>
<tr>
<td>150mg TWICE daily</td>
<td>20mg ONCE daily</td>
<td>5 mg TWICE daily</td>
<td>60mg ONCE daily*</td>
</tr>
<tr>
<td>Reduce dose to:</td>
<td>Reduce dose to:</td>
<td>Reduce dose to:</td>
<td>Reduce dose to:</td>
</tr>
<tr>
<td>110mg TWICE daily</td>
<td>15mg ONCE daily</td>
<td>2.5 mg TWICE daily</td>
<td>30mg ONCE daily</td>
</tr>
<tr>
<td>If 1 or more of the following risk factors:</td>
<td>If the following risk factor:</td>
<td>If 2 or more of the following risk factors:</td>
<td></td>
</tr>
<tr>
<td>• age ≥ 80yrs</td>
<td>• CrCl 15 - 49 ml/min</td>
<td>• CrCl 15 - 49 ml/min</td>
<td></td>
</tr>
<tr>
<td>• taking verapamil</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Or consider reducing based on an individual assessment of the thromboembolic and bleeding risk if the following:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• age 75-80yrs</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• CrCl 30-50ml/min</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• patients with gastritis, oesophagitis or gastroesophageal reflux</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• patients at increased risk of bleeding</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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

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

### Cockcroft-Gault Equation for calculating Creatinine Clearance (CrCl)

\[
\text{CrCl (ml/minute)} = \frac{(140 - \text{age}) \times \text{weight}^*}{\text{Serum Creatinine (micromol/L)}} \times 1.23 \text{ (male)} \text{ or } x 1.04 \text{ (female)}
\]

When calculating CrCl follow the guidance below:

<table>
<thead>
<tr>
<th>Is Patient:</th>
<th>What weight should I use?</th>
<th>The MD+CALC on line calculator can be used to calculate patients CrCl</th>
<th>Which values to use on dose calculator:</th>
<th>What about patients on the cusp of a dose change?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Underweight, normal weight or overweight (BMI &lt;30 kg/m(^2))</td>
<td>Actual body weight (kg)</td>
<td>The MD+CALC on line calculator can be used to calculate patients CrCl</td>
<td>Box 1: Will calculate a CrCl based on patients actual body weight</td>
<td>Where a patient's CrCl places them on the cusp of a dose change it may be particularly important to consider other risk factors such as stroke, bleeding risk, co-morbidities and drug interactions before making a decision.</td>
</tr>
<tr>
<td>Obese or morbidly obese (BMI ≥ 30 kg/m(^2))</td>
<td>Adjusted body weight (ABW)(kg)*</td>
<td></td>
<td></td>
<td>Box 2: Will calculate a CrCl based on patients adjusted body weight (ABW)</td>
</tr>
</tbody>
</table>

*Adjusted body weight = Ideal body weight + 0.4 x (actual body weight – ideal body weight)

### Cockcroft-Gault Equation for calculating Creatinine Clearance (CrCl)

\[
\text{CrCl (ml/minute)} = \frac{(140 - \text{age}) \times \text{weight}^*}{\text{Serum Creatinine (micromol/L)}} \times 1.23 \text{ (male)} \text{ or } x 1.04 \text{ (female)}
\]

### Weight:

The clinical trials of NOACs used actual body weight when estimating CrCl for patients. However, the number of patients with obesity within the NOAC trials were small, in addition it is recognised that there are inaccuracies in estimating CrCl using the Cockcroft-Gault equation at extremes of body weight. Therefore for obese or morbidly obese (BMI ≥ 30 kg/m\(^2\)) patients estimate the CrCl range using adjusted body weight (ABW). This applies an adjustment of 40% of the patient’s excess weight over their ideal body weight (IBW). IBW for men = 50 kg + 2.3 kg for each inch over 5 feet and for women IBW = 45.5 kg + 2.3 kg for each inch over 5 feet.
8. NOAC monitoring and follow-up

All patients on long-term anticoagulants require a general review at least once a year: 10,16

- **Assessment of Stroke and Bleeding Risk**
  - Recalculate CHA\(_2\)DS\(_2\)-VASc and HAS-BLED scores to confirm if risk/benefit remains unchanged
  - Enquire about the presence of bleeding (Nuisance or Impacting on QOL)
  - Identify and minimise any modifiable risk factors
  - Confirm anticoagulation is still appropriate

- **Assess adherence**
  - Re-educate on importance of strict intake schedule
  - Identify any side effects, especially those that may be impacting on compliance

- **Co-medications**
  - Review other medications (inclusive of OTC and herbal medication) for drug interactions
  - See Common drug Interactions with NOACs (Drug interactions with NOACs)

- **Blood sampling and weight**
  - Frequency of follow-up blood tests and weight

<table>
<thead>
<tr>
<th>Patient group</th>
<th>U&amp;Es</th>
<th>Weight</th>
<th>CrCl</th>
<th>FBC</th>
<th>LFTs</th>
<th>BP</th>
<th>Clotting</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline (all patients)</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>CrCl &gt; 60ml/min</td>
<td>Annually</td>
<td>Annually</td>
<td>Annually</td>
<td>Annually</td>
<td>Annually</td>
<td>Annually</td>
<td></td>
</tr>
<tr>
<td>Any of the following:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age ≥ 75 years, frail, CrCl 30 - 60ml/min</td>
<td>6 monthly</td>
<td>6 monthly</td>
<td>6 monthly</td>
<td>Annually</td>
<td>Annually</td>
<td>Annually</td>
<td></td>
</tr>
<tr>
<td>CrCl &lt; 30ml/min or an expected decline in renal function</td>
<td>3 monthly</td>
<td>3 monthly</td>
<td>3 monthly</td>
<td>Annually</td>
<td>Annually</td>
<td>Annually</td>
<td></td>
</tr>
<tr>
<td>Intercurrent condition that may impact renal or liver function</td>
<td>If needed</td>
<td>If needed</td>
<td>If needed</td>
<td>If needed</td>
<td>If needed</td>
<td>If needed</td>
<td></td>
</tr>
</tbody>
</table>

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

INR will not provide information on intensity of anticoagulation effect. INR results for patient on NOACs do not correlate with clinical effect.
9. Warfarin monitoring and follow-up

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

- **Assessment of Stroke and Bleeding Risk**
  - Recalculate CHA₂DS₂-VASc and HAS-BLED scores to confirm if risk/benefit remains unchanged
  - Enquire about the presence of bleeding (Nuisance or Impacting on QOL)
  - Identify and minimise any modifiable risk factors
  - Confirm anticoagulation is still appropriate

- **Assessing anticoagulation control with warfarin**
  Calculate the person’s time in therapeutic range (TTR) at each visit. When calculating TTR:
  - Use a validated measurement method
  - Exclude measurements taken during the first 6 weeks of treatment
  - Calculate TTR over a maintenance period of at least 6 months

- **Reassess anticoagulation for a person with poor anticoagulation control shown by any of the following:**
  - INR values higher than 5 OR 1 INR value higher than 8 within the past 6 months
  - INR values less than 1.5 within the past 6 months
  - TTR less than 65%

- **When reassessing, take into account and if possible address the factors that may contribute to poor control:**
  - Patient education
  - Cognitive function
  - Adherence to prescribed therapy
  - Illness
  - Interacting drugs
  - Lifestyle factors including diet and alcohol
  - Inconvenient/inappropriate monitoring arrangements – confirm suitability and consider self-monitoring and self-management arrangements, consider domiciliary monitoring arrangements for those patients with reduced mobility.

- **For all patients deemed to have failed on warfarin therapy, establish relevant anticoagulant treatment history.**
  Confirm evidence to support proposed reason for treatment failure, for example:
  - Failed monitoring arrangements – did the patient attend an anticoagulant monitoring service?
  - Labile INR – did the patient achieve a therapeutic INR?
  - Bleeding complications – was the bleed major/ minor? Confirm INR at time of bleed.
  - Drug interactions – any change to concurrent therapy should be considered.
  - Serious ADR – was this documented in patient records?
  - Severe alopecia – was the patient offered alternative VKA agents?

- **If poor INR control cannot be improved, evaluate the risks and benefits of alternative stroke prevention strategies and discuss this with the patient.**
10. Communication across secondary/primary care interface - Information to be transferred to GPs

Letters to GPs from secondary care, when anticoagulation has been initiated in secondary care, to include all of the following information:

- Baseline assessment results: CHA$_2$DS$_2$-VASc score, HAS-BLED score, renal function as CrCl, haemoglobin, platelets.
- Discussion with patient/carer:
  - Likelihood of stroke in the individual patient in next year
  - Likelihood of benefit with OAC (NB: It is important that patients/ carer understand that there is never 100% certainty that treated patients will not have a stroke).
  - Likelihood of major bleeding in next year
  - Implications of OAC on major bleeding
  - Choice of OAC. (See Patient information leaflets and clinical decision aid)
- Information to be given to patient:
  - Anticoagulant alert card
  - Information for monitoring bleeds
  - Patient leaflet on oral anticoagulants
Appendix 1: NOAC patient counselling checklist

The following should be discussed with all patients started on oral anticoagulation and should be documented in the patient record.

<table>
<thead>
<tr>
<th>Patient information given (^{4,7,16})</th>
<th>√</th>
</tr>
</thead>
<tbody>
<tr>
<td>Explain purpose.</td>
<td></td>
</tr>
<tr>
<td>Dose and frequency.</td>
<td></td>
</tr>
<tr>
<td>Timing of doses.</td>
<td></td>
</tr>
<tr>
<td>Ensure that rivaroxaban is taken with food. (^{3})</td>
<td></td>
</tr>
<tr>
<td>Duration of treatment.</td>
<td></td>
</tr>
<tr>
<td>Importance of compliance and what to do if doses are missed – see patient information leaflet</td>
<td></td>
</tr>
<tr>
<td>Explain serious side effects</td>
<td></td>
</tr>
<tr>
<td>• Bleeding - Seek urgent medical attention if patient develops severe bleeding, e.g. blood in faeces, vomit or sputum, vaginal bleeding.</td>
<td></td>
</tr>
<tr>
<td>• Advise to seek urgent medical attention if they fall or injure themselves during treatment, especially if they hit their head, due to the increased risk of bleeding.</td>
<td></td>
</tr>
<tr>
<td>• Unusual headaches.</td>
<td></td>
</tr>
<tr>
<td>Need to inform medical staff that they are taking NOAC if prescribed new medications or surgery /or if invasive procedures (including dental extractions) being planned. Bleeding risk if NOAC started immediately post op.</td>
<td></td>
</tr>
<tr>
<td>Possible interactions with other drugs including herbal remedies - advise patient to read patient information leaflet and discuss with pharmacist or doctor before taking any over the counter remedies.</td>
<td></td>
</tr>
<tr>
<td>Avoid aspirin or NSAIDs (unless clinically indicated)</td>
<td></td>
</tr>
<tr>
<td>Advise patient to seek advice if planning to become pregnant or breastfeed</td>
<td></td>
</tr>
<tr>
<td>Referral to Community Pharmacy New Medicines Service (NMS) – suitable for patients prescribed anticoagulants for the first time</td>
<td></td>
</tr>
<tr>
<td>Monitoring and review: review of treatment and blood tests at least once a year but may be more frequent for some patients (see monitoring requirements)</td>
<td></td>
</tr>
<tr>
<td>Alert card and patient information given</td>
<td></td>
</tr>
</tbody>
</table>
### Appendix 2: Switching between oral anticoagulants for non-valvular atrial fibrillation

Consult the Summary of Product Characteristics for each individual anticoagulant for further information. ④7,10,16

<table>
<thead>
<tr>
<th>Switching from</th>
<th>Switching to</th>
<th>Dabigatran (Pradaxa)</th>
<th>Edoxaban (Lixiana)</th>
<th>Rivaroxaban (Xarelto)</th>
<th>Apixaban (Eliquis)</th>
<th>Low Molecular Weight heparin (LMWH)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Warfarin</td>
<td>Warfarin</td>
<td>Discontinue warfarin and start dabigatran: When INR is ≤ 2</td>
<td>Discontinue warfarin and start edoxaban: When INR is ≤ 2.5</td>
<td>Discontinue warfarin and start rivaroxaban: When INR is ≤ 3</td>
<td>Discontinue warfarin and start apixaban: When INR is ≤ 2</td>
<td>Initiate prophylactic or treatment dose LMWH once INR below 2</td>
</tr>
<tr>
<td>Dabigatran (Pradaxa)</td>
<td>Conversion protocol depends on renal function: For CrCl ≥ 50ml/minute, commence warfarin 3 days prior to discontinuing dabigatran. For CrCl 30-50ml/minute, commence warfarin 2 days prior to discontinuing dabigatran. NB: dabigatran can increase INR. INR measurements should be interpreted cautiously until dabigatran has been stopped for 2 days.</td>
<td>Discontinue dabigatran and commence edoxaban at the time that the next dose of dabigatran would be due.</td>
<td>Discontinue dabigatran and commence rivaroxaban at the time that the next dose of dabigatran would be due.</td>
<td>Discontinue dabigatran and commence apixaban at the time that the next dose of dabigatran would be due.</td>
<td>Discontinue dabigatran and commence LMWH 12-hours after the last dose of dabigatran was administered.</td>
<td></td>
</tr>
<tr>
<td>Edoxaban (Lixiana)</td>
<td>Patients on 60 mg dose of edoxaban; administer edoxaban at a dose of 30 mg once daily together with warfarin. Patients 30 mg dose of edoxaban; administer edoxaban at a dose of 15 mg once daily together with warfarin. Measure the INR just prior to the daily dose of edoxaban, continue edoxaban until the INR is ≥ 2.0.</td>
<td>Discontinue edoxaban and commence dabigatran at the time that the next dose of edoxaban would be due.</td>
<td>Discontinue edoxaban and commence rivaroxaban at the time that the next dose of edoxaban would be due.</td>
<td>Discontinue edoxaban and commence apixaban at the time that the next dose of edoxaban would be due.</td>
<td>Discontinue edoxaban and commence LMWH at the time that the next dose of edoxaban would be due.</td>
<td></td>
</tr>
<tr>
<td>Rivaroxaban (Xarelto)</td>
<td>Commence warfarin in combination with rivaroxaban. Rivaroxaban should be discontinued when INR is in therapeutic range. Measure INR prior to each dose of rivaroxaban being administered.</td>
<td>Discontinue rivaroxaban and commence dabigatran at the time that the next dose of rivaroxaban would be due.</td>
<td>Discontinue rivaroxaban and commence edoxaban at the time that the next dose of rivaroxaban would be due.</td>
<td>Discontinue rivaroxaban and commence apixaban at the time that the next dose of rivaroxaban would be due.</td>
<td>Discontinue rivaroxaban and commence LMWH at the time that the next dose of rivaroxaban would be due.</td>
<td></td>
</tr>
<tr>
<td>Apixaban (Eliquis)</td>
<td>Commence warfarin in combination with apixaban. Apixaban should be continued for 2 days, after which point INR should be measured prior to each dose of apixaban. Apixaban should be discontinued when INR is ≥ 2.0.</td>
<td>Discontinue apixaban and commence dabigatran at the time that the next dose of apixaban would be due.</td>
<td>Discontinue apixaban and commence edoxaban at the time that the next dose of apixaban would be due.</td>
<td>Discontinue apixaban and commence rivaroxaban at the time that the next dose of apixaban would be due.</td>
<td>Discontinue apixaban and commence LMWH at the time that the next dose of apixaban would be due.</td>
<td></td>
</tr>
<tr>
<td>Switching from</td>
<td>Switching to</td>
<td>Dabigatran (Pradaxa)</td>
<td>Edoxaban (Lixiana)</td>
<td>Rivaroxaban (Xarelto)</td>
<td>Apixaban (Eliquis)</td>
<td>Low Molecular Weight heparin (LMWH)</td>
</tr>
<tr>
<td>---------------</td>
<td>--------------</td>
<td>----------------------</td>
<td>-------------------</td>
<td>----------------------</td>
<td>-------------------</td>
<td>-----------------------------------</td>
</tr>
<tr>
<td>Low Molecular Weight Heparin (LMWH)</td>
<td>Commence warfarin in combination with LMWH, and monitor INR. Discontinue LMWH once INR in therapeutic range for 2 consecutive days.</td>
<td>Discontinue LMWH and commence dabigatran 0-2 hours before the time that the next dose of LMWH would be due.</td>
<td>Discontinue LMWH and commence edoxaban at the time that the next dose of LMWH would be due.</td>
<td>Discontinue LMWH and commence rivaroxaban 0-2 hours before the time that the next dose of LMWH would be due.</td>
<td>Discontinue LMWH and commence apixaban at the time that the next scheduled dose of LMWH would be due.</td>
<td></td>
</tr>
</tbody>
</table>
## Appendix 3: Comparative costs of NOACs

<table>
<thead>
<tr>
<th>Drug</th>
<th>Usual AF dose</th>
<th>Pack size</th>
<th>List price*</th>
<th>28 day cost per patient</th>
</tr>
</thead>
<tbody>
<tr>
<td>Apixaban</td>
<td>5mg twice daily</td>
<td>56</td>
<td>£53.20</td>
<td>£53.20</td>
</tr>
<tr>
<td>Dabigatran</td>
<td>150mg twice daily</td>
<td>60</td>
<td>£51.00</td>
<td>£47.60</td>
</tr>
<tr>
<td>Edoxaban</td>
<td>60mg daily</td>
<td>28</td>
<td>£49.00</td>
<td>£49.00</td>
</tr>
<tr>
<td>Rivaroxaban</td>
<td>20mg daily</td>
<td>28</td>
<td>£50.40</td>
<td>£50.40</td>
</tr>
</tbody>
</table>

*May 2019 Drug Tariff*
Acknowledgments

Guidelines adapted for local implementation across Hertfordshire from The East of England Priorities Advisory Committee, Atrial fibrillation anticoagulant clinical decision aid v3.1. [https://www.prescqipp.info/our-resources/webkits/pac-eoe/pac-resources/commissioning-recommendations/](https://www.prescqipp.info/our-resources/webkits/pac-eoe/pac-resources/commissioning-recommendations/)


References


https://www.ahajournals.org/doi/full/10.1161/CIRCULATIONAHA.116.022361

https://link.springer.com/article/10.1007/s40262-017-0554-0
