Guidelines for prescribing in primary care: Atrial Fibrillation

Implementation date: September 2014
Review date: September 2016

This guideline has been prepared and approved for used within Gateshead in consultation with Gateshead CCG and Secondary Care Trusts.

Approved by:

<table>
<thead>
<tr>
<th>Committee</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gateshead Medicines Management Committee</td>
<td>14th January 2015</td>
</tr>
</tbody>
</table>

This guideline is not exhaustive and does not override the individual responsibility of health professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.

Full details of contra-indications and cautions for individual drugs are available in the BNF or in the Summary of Product Characteristics (available in the Electronic Medicines Compendium) www.emc.medicines.org.uk
Atrial fibrillation in Primary Care

Estimates suggest the prevalence of atrial fibrillation is increasing and left untreated atrial fibrillation is a significant risk factor for stroke and other morbidities.

**AF – Stroke risk assessment:**

NICE CG180 – Atrial Fibrillation: the management of atrial fibrillation was published in June 2014 and made some significant changes to the diagnosis and treatment of AF.

The overall stroke risk in patients with AF is around 5%. This, however, can vary substantially between patients ranging from a 15-year risk of around 1.3% in younger patients with lone AF up to an annual figure of almost 20% or higher if the individual suffers from valve disease.

NICE now recommends risk is assessed using the CHA2DS2-Vasc and HAS-BLED tools.

### CHA2DS2-Vasc

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Congestive heart failure / LVSD</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 / Thromboembolism</td>
<td>2</td>
</tr>
<tr>
<td>Vascular Disease</td>
<td>1</td>
</tr>
<tr>
<td>Age 65-74</td>
<td>1</td>
</tr>
<tr>
<td>Sex category – Female</td>
<td>1</td>
</tr>
</tbody>
</table>

**Maximum Score** 9

### HAS-BLED

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td>1</td>
</tr>
<tr>
<td>Abnormal Renal / Hepatic Function(^1) - (1 each)</td>
<td>1 or 2</td>
</tr>
<tr>
<td>Stroke</td>
<td>1</td>
</tr>
<tr>
<td>Bleeding</td>
<td>1</td>
</tr>
<tr>
<td>Labile INRs(^2)</td>
<td>1</td>
</tr>
<tr>
<td>Elderly (&gt;65yrs)</td>
<td>1</td>
</tr>
<tr>
<td>Drugs (e.g. NSAIDs) and/or Alcohol (≥8 drinks per week) - (1 each)</td>
<td>1 or 2</td>
</tr>
</tbody>
</table>

**Maximum Score** 9

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\(^1\) Renal Disease - Dialysis, transplant, Cr >2.6 mg/dL or >200 μmol/L

Liver Disease - Cirrhosis, Bilirubin >2x Normal, AST/ALT/AP >3x Normal

\(^2\) Unstable/high INRs, Time in Therapeutic Range < 60%
**Stroke risk:**
These figures are the approximate number per 1000 patients each year whom have AF and who are predicted to still get a stroke.

<table>
<thead>
<tr>
<th>Score</th>
<th>No medication</th>
<th>Warfarin</th>
<th>NOAC</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHA₂DS₂-Vasc =0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CHA₂DS₂-Vasc =1</td>
<td>13</td>
<td>5</td>
<td>4</td>
</tr>
<tr>
<td>CHA₂DS₂-Vasc =2</td>
<td>22</td>
<td>8</td>
<td>6</td>
</tr>
<tr>
<td>CHA₂DS₂-Vasc =3</td>
<td>32</td>
<td>12</td>
<td>9</td>
</tr>
<tr>
<td>CHA₂DS₂-Vasc =4</td>
<td>40</td>
<td>14</td>
<td>10</td>
</tr>
<tr>
<td>CHA₂DS₂-Vasc =5</td>
<td>67</td>
<td>24</td>
<td>18</td>
</tr>
<tr>
<td>CHA₂DS₂-Vasc =6</td>
<td>98</td>
<td>35</td>
<td>25</td>
</tr>
</tbody>
</table>

**HAS-BLED Score:**
These figures are the approximate number per 1000 patients each year who are predicted to have major bleeds (GI or intra-cranial) whilst on anticoagulation.

<table>
<thead>
<tr>
<th>Score</th>
<th>Per 1000 pt per year</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>10</td>
</tr>
<tr>
<td>1</td>
<td>20</td>
</tr>
<tr>
<td>2</td>
<td>30</td>
</tr>
<tr>
<td>3</td>
<td>40</td>
</tr>
<tr>
<td>4</td>
<td>88</td>
</tr>
</tbody>
</table>

**Antiplatelets**

Do not offer antiplatelets as sole treatment for the prevention of stroke in people with atrial fibrillation. Where anticoagulation is not indicated antiplatelets should be stopped.

In cases where an individual has a stent or is post ACS and would normally be treated with dual antiplatelet therapy please discuss on-going treatment of these patients on an individual basis with their consultant cardiologist.

**Choice of anticoagulant**

Key groups in whom newer oral anticoagulation drugs (NOACs) should especially be considered includes:

- Those who cannot take vitamin K antagonists or have declined to take warfarin
• Those who cannot be stabilised on vitamin K antagonists with poor time in therapeutic range (e.g. less than 65% despite adequate adherence). TTR should be calculated over a maintenance time of at least 6 months, excluding measurements taken within the first 6 weeks of treatment
• Those taking aspirin for stroke prevention where an assessment has been made and warfarin may not be suitable due to reasons that would not specifically exclude them from using anticoagulation

There are currently four available anticoagulants, warfarin, apixaban, dabigatran and rivaroxaban. The newer oral anticoagulants should be targeted to patients who are likely to derive greatest benefit.

Primary care rebate schemes exist for dabigatran and rivaroxaban.

The Newer Oral Anticoagulants should only be used for non-valvular AF within product license and in line with the relevant NICE technology appraisals:

• NICE TA275 - Apixaban for preventing stroke and systemic embolism in people with nonvalvular atrial fibrillation
• NICE TA249 - Dabigatran etexilate for the prevention of stroke and systemic embolism in atrial fibrillation
• NICE TA256 - Rivaroxaban for the prevention of stroke and systemic embolism in people with atrial fibrillation

The decision regarding which treatment is to be used should be made after an informed discussion between the clinician and the patient about the risks and benefits of each of the treatments compared with each other and against no treatment at all.

Use of serum creatinine and eGFR estimated with the MDRD equation may result in a misrepresentation of renal function. This is of particular relevance in elderly patients with low body weight (and conversely younger patients with high muscle mass). Therefore, any patients considered for a newer anticoagulant with reduced renal function should have their creatinine clearance more accurately estimated using the Cockcroft-Gault equation:

$$CrCl = \frac{(140 - \text{age}) \times \text{weight (kg)} \times 1.23 \text{ for men or } 1.04 \text{ for women}}{\text{Serum creatinine (µmol/L)}}$$

<table>
<thead>
<tr>
<th>Creatinine Clearance</th>
<th>Apixaban</th>
<th>Dabigatran</th>
<th>Rivaroxaban</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥50ml/min</td>
<td>5mg BD</td>
<td>150mg BD</td>
<td>20mg OD</td>
</tr>
<tr>
<td>30-49ml/min</td>
<td>(or 2.5mg BD if 2 or more of the following are present - &gt;80y, &lt;60kg or serum cr &gt;133mmol/L)</td>
<td>110mg BD</td>
<td>15mg OD</td>
</tr>
<tr>
<td>15-29ml/min</td>
<td>2.5mg BD</td>
<td>Avoid</td>
<td>15mg OD (with caution)</td>
</tr>
<tr>
<td>&lt;15ml/min</td>
<td>Avoid</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Dosages in renal impairment
Individuals stable on warfarin should not routinely be considered for changing to a newer oral anticoagulant. Care should be taken to ensure a safe transition between preparations and advice sought from the patient’s anticoagulation service where appropriate. Further information is also available on the SPC for each of the newer anticoagulants.

For patients using antiplatelets it is not necessary to have a break between stopping the antiplatelet and starting the NOAC and it is safe to start the new medication the day following the last antiplatelet dose.

**NOACs and Compliance aids / swallowing difficulties**

Rivaroxaban may be used in compliance aids and is able to be crushed and administered via feeding tube as per the SPC.

**NOACs and Food**

To ensure appropriate bioavailability rivaroxaban must be given with food. The bioavailability of apixaban and dabigatran are not affected by food.

**NOAC Antidotes**

Although there are currently no specific antidotes for the NOACs the following points should be taken into consideration when prescribing these drugs:

- The half-life of NOACs in patients with normal renal function is between 9-14 hours.
- It takes 4-6 hours to effectively lower INR using vitamin K in patients taking warfarin. Prothrombin complex concentrate (PCC) will reverse warfarin effect immediately.
- Aspirin has no antidote and a similar /higher bleeding risk to a NOAC and a duration of effect of 5-7 days.
- Work to develop specific antidotes for NOACs is in progress.

**Switching between anticoagulants**

*Warfarin to NOAC:*
- Stop warfarin and start NOAC once the INR is <2.0

*NOAC to warfarin:*
- Start warfarin.
- After 2 days if co-administration of warfarin and NOAC obtain INR.
- Discontinue NOAC when the INR is >2.0
Contraindications

Many patients do not receive anticoagulation due to perceived contraindications. However, absolute contraindications are relatively rare and in studies were only found to make up about 7% and the remainder of patients had relative contraindications which do not specifically exclude them from using anticoagulants and many may be able to be treated.

A risk of falls is not a contraindication to initiating an oral anticoagulant. For example; a patient with an annual stroke risk of 5% would need to fall almost 300 times for the risk of falling to outweigh the stroke reduction benefit of an oral anticoagulant.

### Absolute contraindications

- History of inter-cranial haemorrhage
- Existing or recent peptic ulcer disease
- Oesophageal varices
- Previous hypersensitivity / adverse reaction to warfarin
- Advanced malignancy / terminal illness
- BP >180/110 - (reconsider once BP controlled)
- Endocarditis
- Pregnancy
- Platelet count below 50 x 10^9/L

### Relative contraindications

- History of gastro-intestinal haemorrhage
- Unexplained anaemia
- Bleeding diasthesis
- Alcohol abuse
- Renal impairment (Creatinine clearance <15m/min/1.73 is considered an absolute contraindication for all NOACs)
- Hepatic impairment (Child-Pugh rating C could be considered absolute contraindication for all NOACs)
- Adverse drug interaction
- Non-compliance
- Platelet count between 50-150 x 10^9/L

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**Child-Pugh Score**

The Child- Pugh classification is a means of assessing the severity of liver cirrhosis.

<table>
<thead>
<tr>
<th>Score</th>
<th>1</th>
<th>2</th>
<th>3</th>
</tr>
</thead>
<tbody>
<tr>
<td>bilirubin (micromol/l)</td>
<td>&lt;34</td>
<td>34-50</td>
<td>&gt;50</td>
</tr>
<tr>
<td>albumin (g/l)</td>
<td>&gt;35</td>
<td>28-35</td>
<td>&lt;28</td>
</tr>
<tr>
<td>INR</td>
<td>&lt;1.7</td>
<td>1.7-2.3</td>
<td>&gt;2.3</td>
</tr>
<tr>
<td>encephalopathy</td>
<td>none</td>
<td>mild</td>
<td>marked</td>
</tr>
<tr>
<td>ascites</td>
<td>none</td>
<td>mild</td>
<td>marked</td>
</tr>
</tbody>
</table>

If there is primary biliary cirrhosis or sclerosing cholangitis then bilirubin is classified as <68=1; 68-170=2; >170=3.
The individual scores are summed and then grouped as:

- <7 = A
- 7-9 = B
- >9 = C

**Patient information and support**

A variety of patient information leaflets are available to help individuals make a decision whether or not to start an anticoagulant. The Atrial Fibrillation Association has several booklets which are available to download – [www.atrialfibrillation.org.uk](http://www.atrialfibrillation.org.uk)

A patient alert card can be downloaded from [www.NOACforAF.eu](http://www.NOACforAF.eu)
Starting warfarin in AF – slow loading regimen:

Discuss and agree warfarin is appropriate for thrombi-embolic prophylaxis

Confirm there are no contraindications to warfarin (if unsure seek specialist advice)
See tables above for summary of absolute and relative contraindications

Ensure baseline blood tests have been done and results seen - FBC, U&E, Coagulation screen, LFT

Blood results abnormal - take appropriate action
Blood results satisfactory

Arrange monitoring and provide information
Book into INR clinic in 1 week
Give educational leaflet

Prescribe:
Warfarin 1mg daily in the 7 days preceding the INR clinic
Continue aspirin until INR ≥ 1.8 (tell the patient)
Stop other anti-platelets (and aspirin as above) unless special reasons for continuing

Arrange follow up with GP; minimum recommended
- 2m after warfarin initiated
- Annually thereafter

Notes:
Target INR range should be 2-3 (target 2.5) in Primary prevention and 2.5-3.5 in Secondary prevention* for patients with atrial fibrillation. If individual circumstances suggest an alternative range may be required, please discuss with specialist care.
(*Secondary prevention patients are those who have had a thrombotic event whilst concordant with treatment and when INR has been maintained within therapeutic range)
Initiation of NOACs in AF:

Discuss and agree a newer anticoagulant is appropriate for thrombi-embolic prophylaxis

Confirm there are no contraindications to a newer anticoagulant (if unsure seek specialist advice)
See tables above for summary of absolute and relative contraindications

Ensure baseline blood tests have been done and results seen - FBC, U&E, Coagulation screen, LFT,
Measure patient weight (for use in calculating creatinine clearance)

Blood results abnormal - take appropriate action
Blood results satisfactory

Calculate creatinine clearance (CrCl) using Cockcroft-Gault formula
\[
CrCl = \frac{(140 - \text{age}) \times \text{weight (kg)} \times 1.23 \text{ for men or } 1.04 \text{ for women}}{\text{Serum creatinine (\mumol/l)}}
\]

Discuss and initiate appropriate newer anticoagulant taking into account renal function and current medication:
(Dabigatran dose may need to be reduced if used with concomitant amiodarone, quinidine or verapamil - Consult BNF for recommended dosage)

Review any medication which may increase the risk of bleeding
Discontinue any anti-platelets and start NOAC the next day
Provide the patient with newer anticoagulant warning card and ensure this is carried at all times

All patients - Review treatment every 3 months:
  - Check adherence
  - Check for signs of thromboembolism
  - Check for any adverse events / side effects
  - Check for any new prescribed or over-the-counter medication which may be contraindicated
  - Complete patient alert card

If under 75 yrs and eGFR >60ml/min ensure annual U&Es
If 75 yrs or over or GFR <60ml/min ensure 6 monthly U&Es and weight
Re-calculate CrCl if any significant changes
(reduced monitoring to 3 monthly if CrCl is between 15-30ml/min)
Ensure annual LFT and FBC