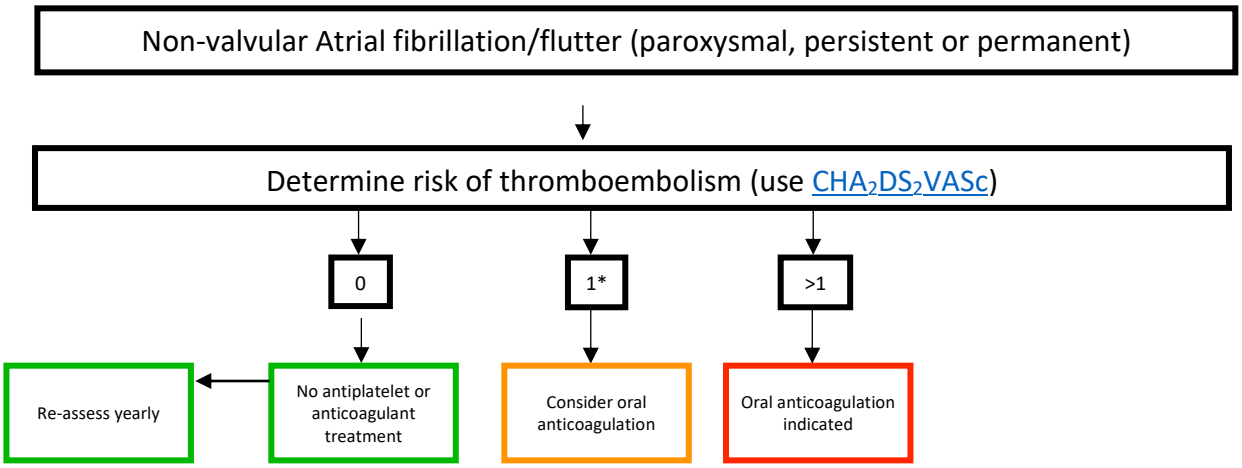
# Anticoagulant treatment for patients with non-valvular atrial fibrillation

Non-valvular atrial fibrillation (NVAF) refers to atrial fibrillation (AF) in the absence of a mechanical prosthetic heart valve or moderate to severe mitral stenosis (usually of rheumatic origin). This guidance also applies to Atrial Flutter.

All Patients need to be assessed for thromboembolic risk with a view to starting anticoagulation.




* A female patient who only scores one point for female gender can be considered to have a score of 0

A bleeding risk assessment tool such as HAS-BLED is recommended, in particular to identify and address modifiable bleeding risk factors.

## Choice of Treatment and Dosing

### Vitamin K Antagonist

### Warfarin

Anticoagulant of choice in;

- Metallic prosthetic valves and moderate to severe mitral stenosis (DOAC contra-indicted as no evidence)
- End stage renal impairment, CrCl <15ml/min
- Hepatic failure (moderate to severe)
- Markedly overweight patients, >120kg or BMI > 40 kg/m$^2$ where DOACS may be less effective
- Antiphospholipid syndrome

In poorly compliant patients warfarin is preferable as at least they are followed up with regular INR monitoring (not a reason to change to a DOAC).

Patients on warfarin who are well controlled (TTR> 65%), should not be switched to a DOAC.

Referral should be made to the NHSL anticoagulation service for initiation and monitoring. Details on how to do this are available through FirstPort under labs/ anticoagulation.

**Direct Oral Anticoagulant (DOAC)**

**Edoxaban** is the NHSL 1st choice DOAC and an alternative DOAC should only be used if there are specific clinical reasons such as;

- History of GI bleeding where apixaban is preferred
- Where renal function:
    - CrCl <15ml/min - warfarin is preferred and DOACs contraindicated
    - CrCl >80ml/min - edoxaban may be less effective and apixaban or warfarin are preferred

**Dose adjustment:** As highlighted in the June 2020 MHRA Drug Safety Alert accurate and up-to-date weight and creatinine are required to calculate the appropriate dose for the patient. The Cockcroft-Gault equation should be used.

**Lab reported eGFR should not be used because it may overestimate renal function and increase the risk of bleeding events.**

- CrCl >50 and <80 ml/min, edoxaban **60mg** daily (unless patient weight <60 kg)
- CrCl >15ml/min and ≤ 50 ml/min, edoxaban **30mg** daily (contraindicated in ≤ 15ml/min
- Weight ≤ 60kg edoxaban **30mg** once daily
- Weight > 120kg see guidance under warfarin

Interactions with other current medicines should be considered carefully (particularly ciclosporin, dronedarone, erythromycin, ketoconazole)

**Apixaban**

**Dose adjustment:**

- Normal dose is 5mg twice daily (when CrCl is 30≥ ml/min)
- Dose reduced to 2.5mg twice daily, if CrCL 15-29 ml/min
- Patients with 2 or more of the following should also be given reduced dose of 2.5mg twice daily:
    - age ≥80 years
    - body weight ≤60kg
    - serum Cr≥133 micromole/l

**Interactions** with other current medicines should be considered carefully (particularly ketoconazole, intraconazole, voriconazole or HIV protease inhibitors)

Patients on DOACs should receive periodic monitoring of renal function and bleeding risk assessment – see appendix 2.

**Additional Good Practice Points**

- Antiplatelet therapy alone is not recommended in AF
- In those already taking antiplatelet therapy the indication for the antiplatelet should be considered carefully:
    - Stroke/TIA – combined antiplatelet therapy no longer indicated.
    - Ischaemic heart disease (IHD)
      In general, antiplatelet therapy can be discontinued in those with stable IHD or in patients > 12 months after MI/stenting (check with Cardiology if duration not clearly noted in patient records).

- Anticoagulation should be used with caution in those with hepatic impairment. In particular, those with deranged coagulation. Seek specialist advice in this situation.

- The decision to use anticoagulation should be a shared one with patients appropriately informed of the risks, benefits and choices available to them. The '5 questions' technique may be used to help structure this discussion with patients. Some guidance on this is provided in appendix 3.

- Patients commenced on anticoagulation should receive appropriate verbal and written education along with an alert card which they should carry at all times - see appendix 1.

- Do not withhold anticoagulants solely because a person is at risk of having a fall

- Pregnancy – Advice should be sought from Obstetrics (may be teratogenic).

Compliance with these medicines is critical regardless of whether a DOAC or warfarin is selected. This should be specially emphasised when counselling patients and is discussed further in appendix

Appendix 1

CHI no ..... DOB ...../...../.....
First name ..... Sex: ☐M ☐F
Last name .....
Address .....
.....
.....
or attach addressograph label here

☐ Hairmyres ☐ Monklands ☐ Wishaw NHS Lanarkshire

# Education Checklist for Patients Receiving Apixaban or Edoxaban

**To be used in conjunction with appropriate education booklet**

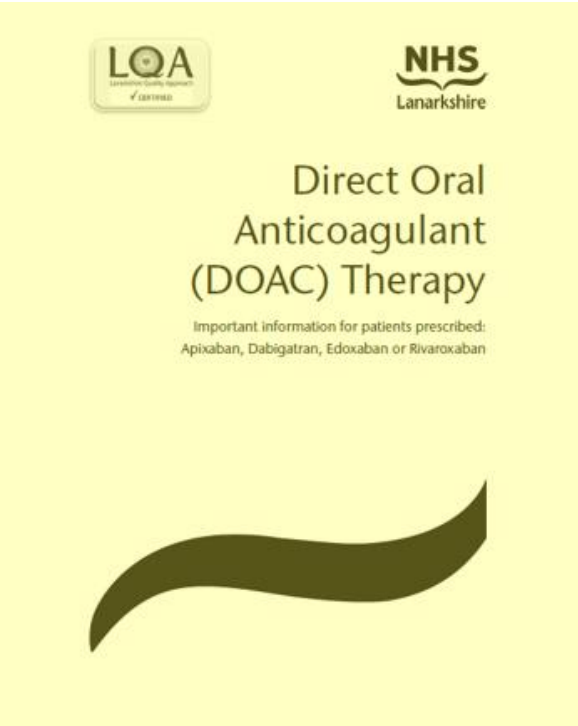
Date: ...../...../.....

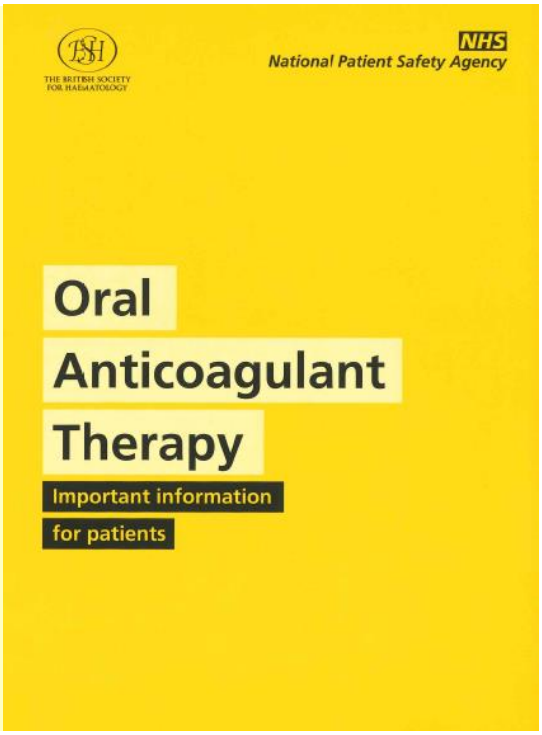
| **Checklist Details/Information** - If there is any doubt about a patient's understanding regarding any part of these instructions, please take note of this and inform prescribing doctor. | **Initial as done** |
|---|---|
| **Manufacturer's booklet**<br>• Give booklet to patient and explain Alert Card *(appropriate to medicine and indication/s)* | |
| **Mode of action**<br>• Explain how medicine blocks a protein involved in blood clotting which reduces the chance of blood clots forming *(Refer to booklet)* | |
| **Reason for therapy**<br>**Patient understands reason(s) for anticoagulation:**<br>☐ Atrial fibrillation (AF); an abnormal heart rhythm associated with an increased risk of stroke<br>☐ Deep vein thrombosis (DVT); a clot in the blood vessels which can lead to a PE<br>☐ Pulmonary embolism (PE); a blood clot in the lungs | |
| **Anticipated length of therapy**<br>**Patient knows proposed length of treatment:**<br>☐ Indefinitely for AF (unless DCCV)<br>☐ PE/DVT - based on individual patient risk factors<br>☐ Other: (specify) ..... | |
| **How to take medication** ☐ Apixaban ☐ Edoxaban<br>**What and when:**<br>• Take as directed on the label.<br>• **In all cases:** - Tablets should be swallowed whole with water.<br>- Try to remember to take at the same time(s) each day. | |
| **Compliance**<br>• This medicine has a short effect (short half life) so omitting doses could cause significant periods of no anticoagulant effect and potentially increase risk of clotting. | |
| **What to do if missed dose**<br>• Take it as soon as you remember - then continue with usual dosing as directed in the manufacturer's booklet.<br>• For Apixaban take as soon as you remember and at the usual times thereafter.<br>• For Edoxaban take as soon as you remember then continue at the usual time from the following day.<br>**What to do if you take too much:**<br>• Contact doctor or pharmacist immediately as taking too much may increase the risk of bleeding. | |
| **Monitoring**<br>• Explain no specific monitoring for this medicine but may need to attend for occasional routine blood tests.<br>• Importance of attending regular doctor appointments.<br>• Importance of monitoring for side effects. | |
| **Side effects**<br>• Advise to specifically look out for symptoms such as bruising and bleeding. Any unexplained bruising or bleeding should be reported to the GP. Seek immediate medical attention if bleeding is severe or prolonged.<br>• Explain when to contact the hospital/GP and how to do this. | |
| **Information for doctors, dentists, pharmacists, etc.**<br>• Explain the importance of informing other health care professionals that the patient is on an oral anticoagulant and the importance of carrying the alert card.<br>• Dentists should be informed of patients taking this medicine.<br>• Check with your pharmacist or doctor before taking any medicines over the counter. | |
| **Advice for women of childbearing age**<br>• Consult doctor before becoming pregnant or visit doctor as soon as possible if believe pregnant or if considering breastfeeding. | |
| **Alcohol considerations**<br>• Explain the interaction between alcohol and anticoagulants and advise to avoid excessive or binge drinking. | |

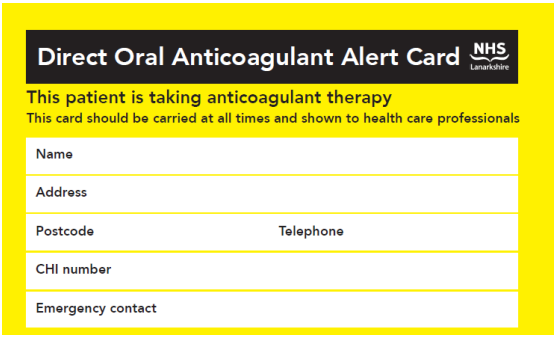
| **Completed by:** | **Signature:** |
|---|---|
| **Patient/Carer:** | **Designation:** |


Pub. date: Oct. 2018 | Review date: Oct. 2021 | Issue No: 01

Approved by ADTC: March 2021 Review date: March 2024
Chair of editorial group: G Lindsay




Approved by ADTC: March 2021
Chair of editorial group: G Lindsay

Review date: March 2024

**Appendix 2 – Monitoring for DOACs**

NB This Guideline is not a formal shared care agreement.

It is recommended that patients receiving DOACs should have their renal function assessed at least once a year and more frequent monitoring is required in clinical situations where renal function may decline and in patients with impaired renal function at baseline.

The European Heart Rhythm Association suggests that in patients with impaired renal function (CrCl <59 ml/min) the recommended frequency of monitoring can be calculated by dividing CrCl by 10 to obtain the minimum frequency of renal function testing in months.

On that basis this guideline recommends the following frequencies for monitoring creatinine clearance:

- CrCl ≥60ml/min – annually
- CrCl 30-59 ml/min – at least 6 monthly
- CrCl 15-29 ml/min – at least 3 monthly
- CrCl less than 15ml/min – DOACs contraindicated

In addition, FBC should be done annually and in order to calculate an accurate CrCl a recent stable weight for the patient (within the last 3-6months) is advised.

| **Severity of renal impairment (creatinine clearance)** | **Edoxaban** | **Apixaban** | **Dabigatran** | **Rivaroxaban** |
|---|---|---|---|---|
| End stage (<15 CrCl mL/Min) | Not recommended | Not recommended | Contraindicated | Not recommended |
| Severe (≤29 CrCl mL/Min) | Dose reduction required in all indications | To be used with caution in some indications; dose reduction is required for other indications | Contraindicated | Use with caution in all indications. Dose adjustment is required or should be considered in some indications |
| Moderate (30–50 CrCl mL/Min) | Dose reduction required in all indications | Dose reduction is required in some indications* | Dose adjustment required or should be considered in some indications | Dose adjustment required or should be considered in some indications |
| Mild (51–80 CrCl mL/Min) | No dose adjustment required | Dose reduction is required in some indications* | No dose adjustment required | No dose adjustment required |

| Severity of renal impairment (creatinine clearance) | Edoxaban | Apixaban | Dabigatran | Rivaroxaban |
|---|---|---|---|---|
| >80 CrCl mL/Min | Should only be used in some indications after a careful evaluation of the individual thromboembolic and bleeding risk | No dose adjustment required | No dose adjustment required | No dose adjustment required |

*In patients with serum creatinine ≥133micromole/L, associated with age ≥80 years or body weight ≤60kg.

## Appendix 3 - decision to commence on anticoagulation

The decision to commence on anticoagulation should be a shared one between the clinician and the patient. This will need to be tailored to the patient and they may require written information to support this. The following 5 questions format can aid a semi-structured conversation with the patient:

- Need? Do I really need this?
  - Overall, AF increases the risk of stroke five-fold.
  - An individual assessment of stroke risk can be calculated using $CHA_2DS_2VASc$. Note this provides the risk of stroke per year.
  - AF related strokes tend to be more severe.

- Benefit? What are the benefits to me?

  - As discussed in the 2020 European Society Guidelines oral anticoagulation significantly reduces stroke (by 64%) and all-cause mortality (by 26%) compared with control or placebo.

- Risk? Are there any risks or side effects?
  - Bleeding is the major side effect of anticoagulation. Most people will encounter some minor bleeding, e.g. more severe bruising as a result of an injury, however more serious bleeding is uncommon.
  - A high bleeding risk score should not lead to withholding anticoagulation, as the net clinical benefit is even greater amongst such patients. However, the formal assessment of bleeding risk informs management of patients taking oral anticoagulants, focusing attention on *modifiable* bleeding risk factors that should be managed and (re)assessed at every patient contact.

- Choice?
  - DOACs have been demonstrated to be non-inferior to warfarin. Patients may be drawn to either a DOAC or warfarin. The following points may help guide this discussion.

| DOAC | Warfarin |
|---|---|
| No requirement for routine anticoagulation monitoring | Can be monitored in anticoagulant clinic |
| Simpler dosing regimen | Individual missed doses less of a concern |
| Less food/drug interactions | Widely available reversal agents |

- If I don't?

  - Increased risk of thromboembolism and stroke with the risk being cumulative with passage of time and increasing with age.

## Appendix 4 – compliance

Shorter half-life of DOACs compared to warfarin

Please see the table below with the approximate half-lives of the 4 DOACs and warfarin:

| | |
|---|---|
| Edoxaban | 10-14 hours |
| Apixaban | 12 hours |
| Rivaroxaban | 5-13 hours |
| Dabigatran | 13-18 hours |
| Warfarin | 40 hours |

If a patient is non-compliant with warfarin, it is important to establish the reasons, e.g. If the patient (with family/friend support if needed) cannot manage the warfarin regime due to a complex regime of different doses on different days, it may be appropriate to switch to a DOAC (as long as no contraindications) to support compliance.

However, if a patient is generally non-compliant with medicines then switching the patient to a DOAC is not the solution and with the shorter half-lives of the DOACs, the patient may then have less protection from thrombotic events and stroke if they are non-compliant with a DOAC compared to warfarin.

For these patients, other measures such as involving family members, friends or carers to assist with compliance should be considered. The impact of this can be monitored using the patient's INR.

Some patients use a pharmacy-filled dosette box, and most DOACs may be housed within such a device (Dabigatran not suitable) but this is not an assured solution and where compliance is essential the potential advantages and disadvantages of this need to be worked through.

It is important to understand that if the patient requires a formal service to administer medication, then Care at Home services cannot provide this for warfarin. But, for patients who require warfarin and already have a Care at Home package in place, there is the potential to switch to a DOAC and for this to be supported by Care at Home.

Warfarin poor anticoagulation control

Patients on warfarin whose time in the therapeutic range (TTR) is <65% should be reviewed. If efforts to improve this by dealing with potential causes prove unsuccessful, then switching to a DOAC should be considered as long as poor compliance is not the cause.

## References/further reading


Akinwunmi, F. (2011) *What you need to know about warfarin.* Pharmaceutical Journal. https://www.pharmaceutical-journal.com/download?ac=1065107&firstPass=false

Bayer plc (2019) *Summary of Product Characteristics for Xarelto.* https://www.medicines.org.uk/emc/product/2793/smpc

Boehringer Ingelheim Limited (2020) *Summary of Product Characteristics for Pradaxa.* https://www.medicines.org.uk/emc/product/4703/smpc

Bristol-Myers Squibb-Pfizer (2020) *Summary of Product Characteristics for Eliquis.* https://www.medicines.org.uk/emc/product/2878/smpc

Daiichi Sankyo UK Limited (2020) *Summary of Product Characteristics for Lixiana.* https://www.medicines.org.uk/emc/product/6906/smpc

European Heart Rhythm Association (2018) *The 2018 European Heart Rhythm Association Practical Guide on the use of non-vitamin K antagonist oral anticoagulants in patients with atrial fibrillation* https://academic.oup.com/eurheartj/article/39/16/1330/4942493

Gerhard Hindricks, Tatjana Potpara, Nikolaos Dagres, et al. (2020) *ESC Guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association of Cardio-Thoracic Surgery (EACTS): The Task Force for the diagnosis and management of atrial fibrillation of the European Society of Cardiology (ESC) Developed with the special contribution of the European Heart Rhythm Association (EHRA) of the ESC*, European Heart Journal, , ehaa612, https://doi.org/10.1093/eurheartj/ehaa612

Jan Steffel, Peter Verhamme, Tatjana S. Potpara, et al. (2018) *The 2018 European Heart Rhythm Association Practical Guide on the use of non-vitamin K antagonist oral anticoagulants in patients with atrial fibrillation. European Heart Journal* 39, 1330–1393. Available online

K. MARTIN, J. BEYER-WESTENDORF, B. L. DAVIDSON, M. V. HUISMAN,§ P. M. SANDSET and S. MOLL (2016) *RECOMMENDATIONS AND GUIDELINES - Use of the direct oral anticoagulants in obese patients: guidance from the SSC of the ISTH* https://onlinelibrary.wiley.com/doi/epdf/10.1111/jth.13323

Medicines and Healthcare Regulatory Agency (2019) *Direct-acting oral anticoagulants (DOACs): increased risk of recurrent thrombotic events in patients with antiphospholipid syndrome.* https://www.gov.uk/drug-safety-update/direct-acting-oral-anticoagulants-doacs-increased-risk-of-recurrent-thrombotic-events-in-patients-with-antiphospholipid-syndrome

Medicines and Healthcare Regulatory Agency (2020) *Direct-acting oral anticoagulants (DOACs): reminder of bleeding risk, including availability of reversal agents.* https://www.gov.uk/drug-safety-update/direct-acting-oral-anticoagulants-doacs-reminder-of-bleeding-risk-including-availability-of-reversal-agents

National Institute for Health and Care Excellent (2018) *Atrial Fibrillation.* https://www.nice.org.uk/guidance/qs93/chapter/quality-statement-4-anticoagulation-control

Specialist Pharmacy Service (2019) *Direct Acting Oral Anticoagulants (DOACs) in Renal Impairment: Practice Guide to Dosing Issues.* https://www.sps.nhs.uk/wp-content/uploads/2019/07/DOAC-dosing-in-renal-impairment-vs2-July-2019-AW.pdf



Approved by ADTC: March 2021 Review date: March 2024
Chair of editorial group: G Lindsay