AF Oral Anticoagulant FAQs

Q: How do I define Valvular / Non valvular Atrial Fibrillation and does this affect the choice of anticoagulant offered to the patient?

Valvular AF refers to AF that occurs in the presence of mechanical prosthetic heart valves or moderate-to-severe mitral stenosis (usually of rheumatic origin). (ESC guidelines of the management of atrial fibrillation 2016 http://www.heartrhythmalliance.org/files/files/afa/for-clinicians/2016%20ESC%20Guidelines.pdf)

- **DOACs are licensed for the prevention of stroke and systemic embolism in adult patients with non-valvular atrial fibrillation (NVAF). As such they may be used in patients with aortic valve stenosis / regurgitation and / or mitral valve regurgitation.**
  - **DOACs should not be used for patients with**
    - **mechanical prosthetic heart valves**
    - **TAVR (**transcatheter aortic valve replacement)
    - **Moderate to severe mitral stenosis.**
- **Vitamin K antagonist (i.e. warfarin) therapy is recommended for stoke prevention in AF patients with moderate-to-severe mitral stenosis or mechanical heart valves.**

Q: Is Aspirin/Clopidogrel monotherapy for stoke prevention a reasonable choice for my patient with atrial fibrillation?

Nice CG180 (June 2014) National Institute for Health and Clinical Excellence (2014) Atrial fibrillation: management. Clinical Guideline 180. London: NICE https://www.nice.org.uk/guidance/cg180/evidence/atrial-fibrillation-update-full-guideline-243739981

- **Do not offer aspirin monotherapy solely for stroke prevention to people with atrial fibrillation.**

For people at increased risk of stroke the use of anticoagulants (compared to single antiplatelet therapy) decreases the risk of all-cause mortality and ischaemic stroke and moderately decreases the risk of systemic emboli.

Q: Should my patient be prescribed aspirin/ clopidogrel whilst on an oral anticoagulant (OAC) for AF?

Combinations of oral anticoagulants and platelet inhibitors increase bleeding risk and should be avoided in AF patients without another indication for platelet inhibition.

- **The decision to continue aspirin /clopidogrel with an OAC for AF should be reviewed on an individual basis for each patient.**
- **The ESC and EHRA guidelines recommend OAC monotherapy, and not combination therapy with antiplatelets, in AF patients with stable Coronary Artery Disease who have not had an Acute Coronary Syndrome (ACS) and / or coronary intervention / stent in the previous 12 months.**

Further advice for individual cases should be sort from local cardiology services

Q: How do I counsel a patient on their stroke risk and the benefit of taking an oral anticoagulant in reducing that risk?

A number of patient decision aids are available to aid discussion with the patient about their individual risk of a stroke- these include:

NICE patient decision aid "**Atrial fibrillation: medicines to help reduce your risk of a stroke – what are the options?**" - https://www.nice.org.uk/guidance/cg180/resources/cg180-atrial-fibrillation-update-patient-decision-aid-243734797

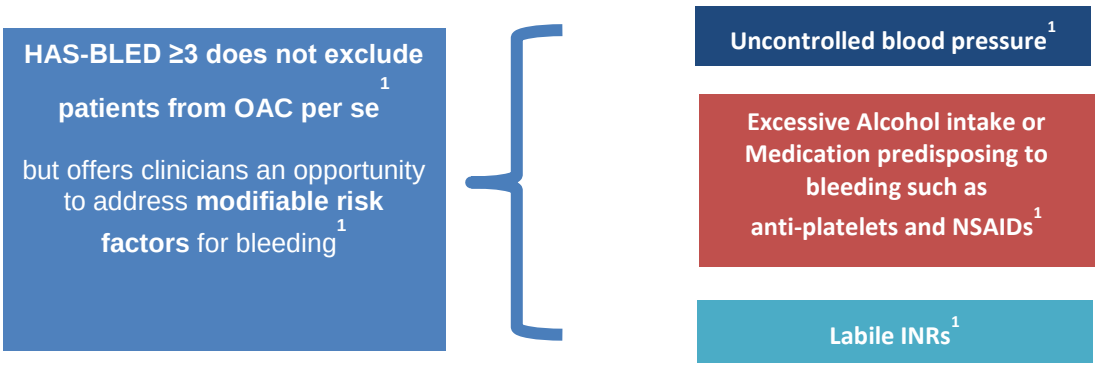
SPARC - Stroke Prevention in Atrial Fibrillation Risk Tool - http://www.sparctool.com/

The below table is adapted from the NICE Patient decision Aid showing the risk of AF-related ischaemic stroke **over 1 year** in a group of **1000** people with atrial fibrillation.

CHA2DS2-VASc score	AF related stroke if NO treatment	AF related stroke on Anticoagulant	No. of strokes prevented
1	6	2	4
2	25	8	17
3	37	12	25
4	55	17	38
5	84	27	57

Q. How do I identify modifiable risk factors for bleeding in patients for consideration of Anticoagulation?

- **NICE / ESC recommends the use of the HAS-bled score[1] to identify risk factors for bleeding. A high bleeding risk score should generally not result in withholding OAC, rather bleeding risk factors should be identified and treatable factors corrected**



(. [1] Kirchhof P, et al. *Eur Heart J* 2016; 37:2893–296)

Q: Can I prescribe Anticoagulation in patients with Cognitive impairment?

- **If a patient is currently receiving medication for primary or secondary prevention of a condition (such as a statin - for hyperlipidaemia) then consideration must be given to**

initiating an anticoagulant. The choice of anticoagulant must reflect the patient's ability to adhere to monitoring requirements as well as any concordance issues.

Q: If Patient has previously refused anticoagulation then what is recommended.

A decision not to treat a patient at increased risk of stroke with an anticoagulant, should be regularly reviewed (at least annually)

If Patient refused due to monitoring requirements of warfarin

- **Consider use of DOAC for the patient as part of an informed patient discussion regarding risk benefit of anticoagulation.**

If Patient refused DOAC due to lack of antidote

- **There is now a licensed antidote for Dabigatran (Idarucizumab) available in hospitals with an Emergency Department in Wales.**

Q: Can I offer anticoagulation to patient with previous GI bleed?

- **The decision to anticoagulate these patients should be reviewed and consideration should be given to initiating a DOAC with a lower gastric bleeding risk than warfarin- such as Apixaban.**

Q: Can I prescribe a DOAC in Patients with liver impairment?

Medicine	Rivaroxaban[2]	Apixaban[3]	Dabigatran[4]	Edoxaban[5]
Use in hepatic impairment	Contraindicated in patients with hepatic disease associated with coagulopathy and clinically relevant bleeding risk including cirrhotic patients with Child Pugh B and C	Prior to initiating apixaban, liver function testing should be performed. Contraindicated in patients with hepatic disease associated with coagulopathy and clinically relevant bleeding risk. Not recommended in patients with severe hepatic impairment. Caution in patients with mild or moderate hepatic impairment (Child Pugh A or B), but no dose adjustment is required. Caution in patients with elevated liver enzymes (ALT/AST >2 x ULN) or total bilirubin ≥1.5 x ULN as these patients were excluded in clinical trials.	Contraindicated in hepatic impairment or liver disease expected to have any impact on survival Not recommended in mild-moderate hepatic impairment with liver enzymes >2 ULN.	Contraindicated in patients with hepatic disease associated with coagulopathy and clinically relevant bleeding risk. Not recommended in patients with severe hepatic impairment. Use with caution in patients with mild-moderate hepatic impairment with liver enzymes >2 ULN or total bilirubin >1.5ULN.

ULN= Upper limit of normal

[2]SmPC- Rivaroxaban accessed 10/12/18 - https://www.medicines.org.uk/emc/product/2793/smpc [3] SmPC- Apixaban accessed 10/12/18 - https://www.medicines.org.uk/emc/product/2878/smpc
[4] SmPC- Dabigatran accessed 10/12/18 - https://www.medicines.org.uk/emc/product/4703/smpc [5] SmPC- Edoxaban accessed 10/12/18 - https://www.medicines.org.uk/emc/product/6905/smpc

Q: Which Anticoagulant / dose of anticoagulant should be prescribed for patients with renal impairment?

Calculated CrCl (ml/min)	≥80	50-79	30-49	15-29	<15
Apixaban	**5mg BD** Reduce dose to 2.5mg BD if ≥2 if: • Age ≥80 years • Weight ≤ 60kg • Serum creatinine > 1.5mg/dl (133µmol/L)			**2.5mg BD** **Used with Caution [1]**	**Not recommended**
Dabigatran	**150mg BD** Reduce dose to 110mg BD if: • Age ≥80 years • Patient on concomitant Verapamil Consider dose reduction if: • Age 75-80 Years • CrCl 30-50 ml/min • Patient at increased bleeding risk or history of gastritis, oesophagitis or GORD			**Not recommended**	
Edoxaban	**60mg OD** Reduce dose to 30mg OD if: • Weight ≤ 60kg • Patient on concomitant P-gp inhibitor		**30mg OD**	**30mg OD** **Use with caution [2]**	**Not recommended**
Rivaroxaban	**20mg OD**		**15mg OD**	**15mg OD** **Use with caution[3]**	**Not recommended**
Warfarin	**As per INR**				

Dose reduction if additional risk factors

Dose reduction based on CrCl

Dose reduction based on CrCl- used with caution see notes

Wafarin is an option for the prevention of strokes in patients with AF

[1] **SPC for Apixaban** - For the prevention of stroke and systemic embolism in patients with NVAF, patients with severe renal impairment (creatinine clearance 15-29 mL/min), and patients with serum creatinine ≥ 1.5 mg/dL (133 micromole/L) associated with age ≥ 80 years or body weight ≤ 60 kg should receive the lower dose of apixaban 2.5 mg twice daily- **However limited clinical experience**

[2] **SPC for Edoxaban- In** patients with moderate (creatinine clearance 30 - 49 ml/min) or severe (creatinine clearance 15 - 29 ml/min) renal impairment or body weight <60kg, for the prevention of stroke and systemic embolism in patients with non-valvular atrial fibrillation, the recommended dose is 30 mg once daily. **However limited clinical experience**

[3] **SPC for Rivaroxaban-** In patients with moderate (creatinine clearance 30 - 49 ml/min) or severe (creatinine clearance 15 - 29 ml/min) renal impairment, for the prevention of stroke and systemic embolism in patients with non-valvular atrial fibrillation, the recommended dose is 15 mg once daily. **However limited clinical experience**

Further information regarding dosing of DOACS in renal impairment:

https://www.sps.nhs.uk/articles/practice-guide-to-dosing-of-direct-acting-oral-anticoagulants-in-patients-with-renal-impairment/

Q: How frequently should I monitor renal function for patient on a DOAC?

CrCl ml/min	Frequency of renal function monitoring required
≥60ml /min	Yearly- unless current condition may impact renal function
50-59 ml/min	Every 5 months- unless current condition may impact renal function
40-49 ml/min	Every 4 months- unless current condition may impact renal function
30-39 ml/min	Every 3months- unless current condition may impact renal function
20-29 ml/min	Minimum of every 2 months

Adapted from EHRA practical guide https://academic.oup.com/eurheartj/article/39/16/1330/4942493

Q: Can I prescribe a DOAC in patients at extremes of body weight?

- **ISTH guidelines recommend not using a DOAC in a patient > 120kg or BMI >40**
  - However, there is increasing experience in using DOACs in patients who weigh > 120kg
  - The International guidelines state that if a DOAC is commenced in a patient with a BMI > 40 or weight > 120kg then measure a peak and trough drug level and if the level falls within the expected range, consensus opinion from the International guidelines is to continue the DOAC. https://onlinelibrary.wiley.com/doi/epdf/10.1111/jth.13323

- ***Anticoagulation (warfarin or DOAC) in patients <50 kg should be used with caution***

Q: Should I offer anticoagulation to a patient with a diagnosis of Paroxysmal atrial fibrillation (PAF)

- **Patients with PAF—as a group—appear to have a risk for embolic events that is at least similar to that of patients with persistent AF. These patients should therefore be treated as having AF for the purposes of OAC consideration.**
- **Presently there is no consensus as to how OAC should be used in an apparently isolated episode of PAF secondary to an underlying condition (e.g. hyperthyroidism or pneumonia). In general OAC therapy similar to other patients with PAF is recommended.**

Further advice for individual cases should be sort from local cardiology services

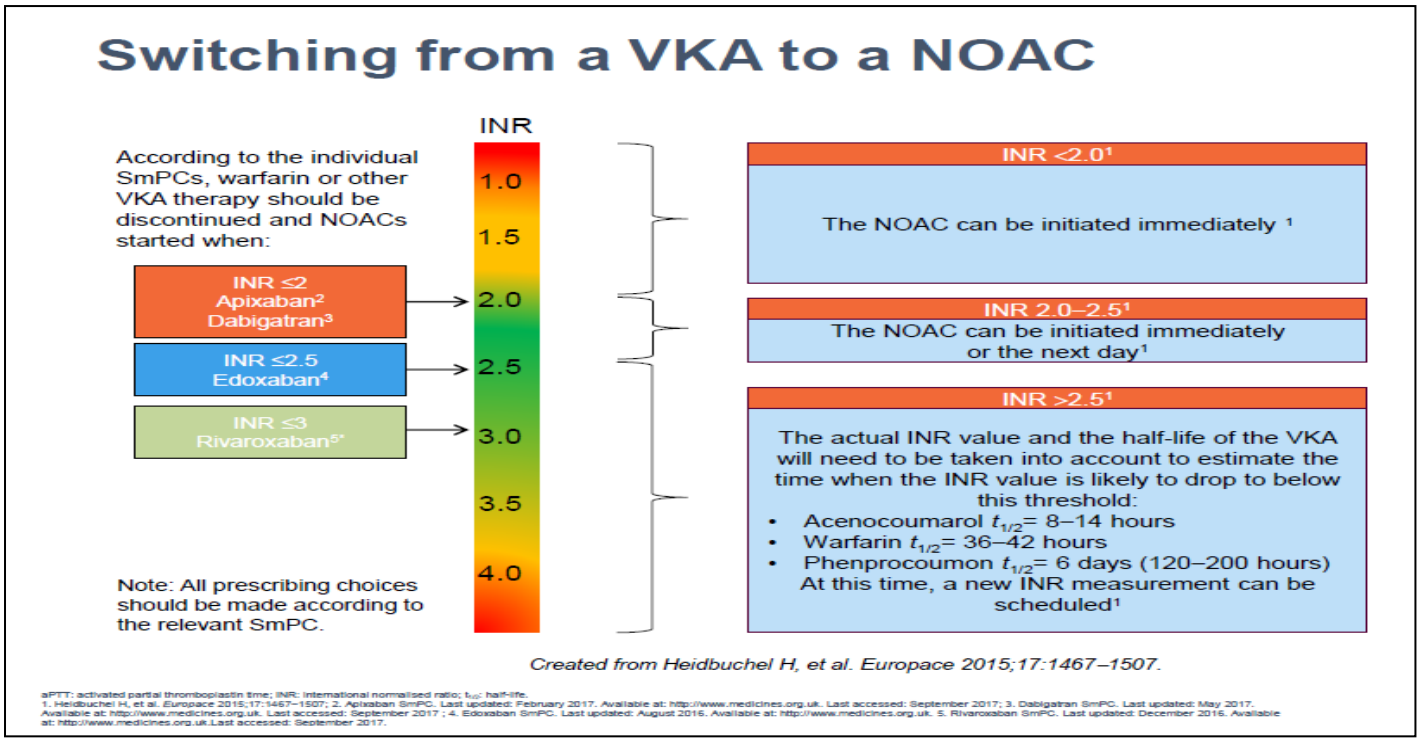
Q: Should I consider anticoagulation for a patient with a history of falls?

Nice CG180 (June 2014) National Institute for Health and Clinical Excellence (2014) Atrial fibrillation: management. Clinical Guideline 180. London: NICE https://www.nice.org.uk/guidance/cg180/evidence/atrial-fibrillation-update-full-guideline-243739981

- **Do not withhold anticoagulation solely because the person is at risk of having a fall.**

History of mechanical falls is not a contra-indication to initiating anticoagulation. Consideration should be given to the cause of the fall(s) and whether a physiological reason for the falls has been excluded.

Q: How do I switch a patient from a VKA to a DOAC?



aPTT: activated partial thromboplastin time; INR: international normalised ratio; $t_{1/2}$: half-life.
1. Heidbuchel H, et al. Europace 2015;17:1467–1507; 2. Apixaban SmPC. Last updated: February 2017. Available at: http://www.medicines.org.uk. Last accessed: September 2017; 3. Dabigatran SmPC. Last updated: May 2017. Available at: http://www.medicines.org.uk. Last accessed: September 2017 ; 4. Edoxaban SmPC. Last updated: August 2016. Available at: http://www.medicines.org.uk. 5. Rivaroxaban SmPC. Last updated: December 2016. Available at: http://www.medicines.org.uk.Last accessed: September 2017.

Q: Can I prescribe a DOAC in patients with thrombocytopenia (low platelet count)?

- Thrombocytopenia is defined as a platelet count < 150 x 10^9/l

Differential diagnosis includes *immune peripheral consumption (ITP),* any cause of *bone marrow failure* (aplasia, malignant infiltration, myelodysplasia, B12 / folate deficiency), *alcohol*, *medication*, *sepsis*, *hypersplenism*, *disseminated intravascular coagulation (DIC)* and *TTP / HUS*.

- Patients with known ITP should be referred to their haematologist to discuss anticoagulation

The following should be referred urgently for haematology assessment:

- Platelet count < 50 x 10^9/l
- Platelet count 50 - 100 x 10^9/l in association with:
  - other cytopenia (Hb < 10g/dl, Neutrophils < 1 x 10^9/l) or
  - splenomegaly, lymphadenopathy, pregnancy, upcoming surgery

Appropriate investigation in primary care for patients not meeting criteria for urgent referral (Platelet count 100-150 x 10^9/l**):**

- Blood film examination – may exclude platelet clumping artefact
- Thyroid function tests
- B12/ folate and ferritin levels
- Liver biochemistry
- Alcohol history
- Consider discontinuation of potentially precipitating medications
- Repeat FBC in 4-6 weeks

- Following appropriate investigations, patients with a stable platelet count of 100 – 150 x 10^9/l, can be commenced on anticoagulation

Q; Are there any definite contra-indications to anticoagulation?

- ***Absolute Contraindications***

- Known large oesophageal varices.
- Significant thrombocytopenia (platelet count < 50 x 109/L) - *refer to haematologist.*
- Within 72 hours of major surgery with risk of severe bleeding - *defer & reassess risk postoperatively.*
- Previously documented hypersensitivity to either the drug or excipients
- Acute clinically significant bleed - *defer & re-assess stroke versus bleeding risk within 3 months.*
- Decompensated liver disease or deranged baseline clotting screen (INR>1.5)
- Pregnancy or within 48 hours post partum - *seek urgent haematological advice.*
- Severe renal impairment (depending on selected Anticoagulant) ***–see above advice***
- Sustained uncontrolled hypertension: systolic blood pressure **≥180 mmHg** or diastolic blood pressure **≥100 mmHg** [1,2,3]

1. https://www.nejm.org/doi/suppl/10.1056/NEJMoa1009638/suppl_file/nejmoa1009638_protocol.pdf
2. https://www.nejm.org/doi/suppl/10.1056/NEJMoa1107039/suppl_file/nejmoa1107039_protocol.pdf
3. https://www.nejm.org/doi/suppl/10.1056/NEJMoa0905561/suppl_file/nejm_connolly_1139sa1.pdf