NHS

County Durham & Tees Valley
Area Prescribing Committee

Prescribing Guideline for the Use of Anticoagulants in Non-Valvular Atrial Fibrillation

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This guideline is intended for use in primary care and only refers to the use of anticoagulants in patients with Non-Valvular Atrial Fibrillation (NVAF).

NVAF refers to atrial fibrillation in the absence of a mechanical prosthetic heart valve or moderate to severe mitral stenosis (usually of rheumatic origin).

It does NOT cover other indications (e.g. mechanical heart valves, VTE)

SUMMARY OF UPDATES FROM NICE GUIDELINE NG196
ATRIAL FIBRILLATION DIAGNOSIS AND MANAGEMENT (updated 30/06/2021)
https://www.nice.org.uk/guidance/ng196

Atrial fibrillation is the most common heart rhythm disorder (affecting approximately 2% of the adult population), and estimates suggest its prevalence is increasing. Atrial fibrillation causes palpitations and breathlessness in many people but it may be asymptomatic and undetected. If left untreated it is a significant risk factor for stroke and other morbidities: it is estimated that it is responsible for approximately 20% of all strokes and is associated with increased mortality. Men are more commonly affected than women and the prevalence increases with age and in underlying heart disease, diabetes, obesity and hypertension.

The aim of treatment is to prevent complications, particularly stroke, and alleviate symptoms. Drug treatments include anticoagulants to reduce the risk of stroke and antiarrhythmics to restore or maintain the normal heart rhythm or to slow the heart rate in people who remain in atrial fibrillation.

This update focuses on areas of new evidence and changing practice since the 2014 NICE guideline. These include methods of assessing stroke and bleeding risk; identifying antithrombotic agents; and preventing recurrence. The recommendations apply to adults (18 years or older) with non-valvular atrial fibrillation (NVAF), including paroxysmal (recurrent), persistent and permanent atrial fibrillation, and atrial flutter. They do not apply to people with congenital heart disease precipitating atrial fibrillation.

- Use the CHA_2DS_2-VASc stroke risk score to assess stroke risk in people with continuing risk of arrhythmia recurrence after cardioversion back to sinus rhythm or catheter ablation.
- Evidence shows that the ORBIT bleeding risk score has a higher accuracy in predicting absolute bleeding risk than other bleeding risk tools. Although ORBIT is the best tool for this purpose, other bleeding risk tools such as HAS-BLED may need to be used until ORBIT is embedded into clinical systems.
- Offer monitoring and support to modify risk factors for bleeding, including reversible causes of anaemia.
- Discuss the results of the assessments of stroke and bleeding risk with the person taking into account their specific characteristics, for example comorbidities, and their individual preferences.
- For people with an increased risk of bleeding, the benefit of anticoagulation may not always outweigh the bleeding risk and so careful monitoring is important.
- When deciding between anticoagulation treatment options, take into account any contraindications for each drug and follow guidance in the BNF and the MHRA advice on direct-acting oral anticoagulants, in particular for advice on dosages in people with renal impairment, reversal agents and monitoring.
- Offer anticoagulation with a direct-acting oral anticoagulant (DOAC) in preference to a VKA (Warfarin) to people with NVAF and a CHA_2DS_2-VASc score of 2 or above, taking into account the risk of bleeding. Apixaban, dabigatran, edoxaban and rivaroxaban are all recommended as options.
- Consider anticoagulation with a direct-acting oral anticoagulant for men with NVAF and a CHA_2DS_2-VASc score of 1, taking into account the risk of bleeding. Apixaban, dabigatran, edoxaban and rivaroxaban are all recommended as options.
- If direct-acting oral anticoagulants are contraindicated, not tolerated or not suitable in people with NVAF, offer a vitamin K antagonist.
- For adults with NVAF who are already taking a vitamin K antagonist and are stable, continue with their current medication and discuss the option of switching treatment at their next routine appointment, taking into account the person's time in therapeutic range.
- Do not offer stroke prevention therapy with anticoagulation to people aged under 65 years with NVAF and no risk factors other than their sex (that is, very low risk of stroke equating to a CHA_2DS_2-VASc score of 0 for men or 1 for women).
- Do not withhold anticoagulation solely because of a person's age or their risk of falls.
- In people with a diagnosis of NVAF, do not stop anticoagulation solely because atrial fibrillation is no longer detectable.
- Base decisions to stop anticoagulation on a reassessment of stroke and bleeding risk using CHA_2DS_2-VASc and ORBIT and a discussion of the person's preferences.

ASSESSMENT OF STROKE & BLEEDING RISK

Use the **CHA_2DS_2-VASc** tool to assess stroke risk in people with any of the following:

- Symptomatic or asymptomatic paroxysmal, persistent or permanent NVAF
- Atrial flutter
- A continuing risk of arrythmia recurrence after cardioversion back to sinus rhythm or catheter ablation

CHA_2DS_2-VASc Score:

Feature	Score
Congestive Heart Failure / LV dysfunction	+1
Hypertension	+1
Age >75 years	+2
Diabetes mellitus	+1
Stroke/TIA/Thromboembolism	+2
Vascular disease (previous MI, peripheral artery disease or aortic plaque)	+1
Age between 65 and 74 years	+1
Sex category - Female	+1

Score	% Annual Risk of Ischemic Stroke	% Annual Risk of Stroke / TIA / Systemic Embolism
0	0.2	0.3
1	0.6	0.9
2	2.2	2.9
3	3.2	4.6
4	4.8	6.7
5	7.2	10.0
6	9.7	13.6
7	11.2	15.7
8	10.8	15.2
9	12.2	17.4

Use the **ORBIT** tool to assess bleeding risk when:

- considering starting anticoagulation in people with NVAF and,
- reviewing people already taking anticoagulation

ORBIT Score:

Risk Factor for Bleeding	Score
Older Age (≥75 years)	+1
Reduced haemoglobin, reduced haematocrit, or history of anaemia (Hb <13 g/dL in men and <12 g/dL in women) (Hct <40% in men and <36% in women)	+2
Bleeding history (any history of GI bleeding, intracranial bleeding or haemorrhagic stroke)	+2
Impaired kidney function (eGFR < 60mL/min/1.73 m^2)	+1
Treatment with an antiplatelet agent	+1

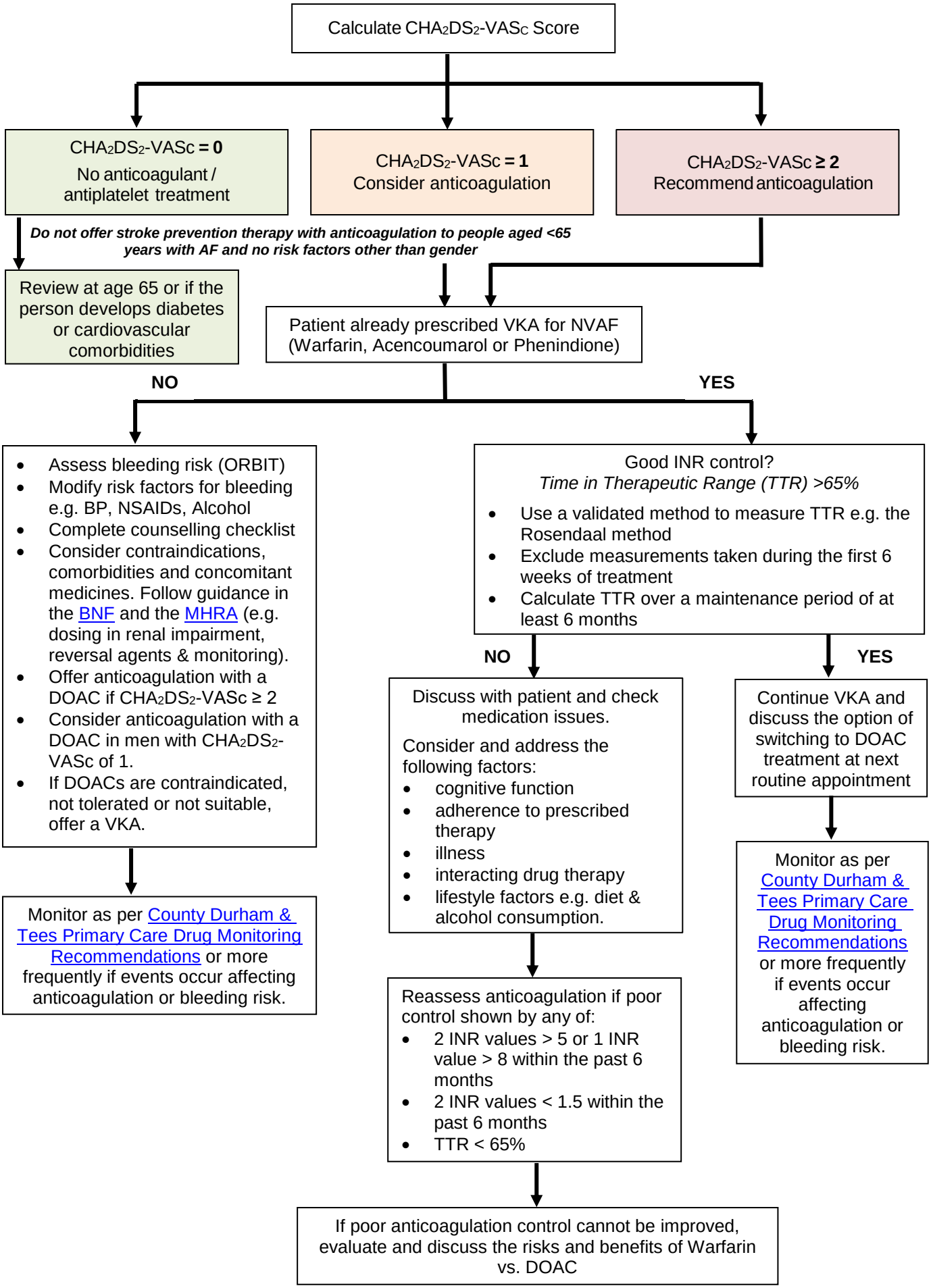
ORBIT Score	Risk group	Bleeds per 100 patient-years
0-2	Low	2.4
3	Medium	4.7
4-7	High	8.1

Other risk factors not part of the ORBIT Score may influence the decision for anticoagulation. Patient preferences and values should go into the decision regarding anticoagulation as it pertains to risks vs benefits of being on anticoagulation for stroke prevention in patients with NVAF.

Offer monitoring and support to modify risk factors for bleeding, including:

- uncontrolled hypertension (systolic BP >160)
- poor control of international normalised ratio (INR) in patients on vitamin K antagonists (TTR <65%)
- concurrent medication, including antiplatelets, selective serotonin reuptake inhibitors (SSRIs) and non-steroidal anti-inflammatory drugs (NSAIDs)
- harmful alcohol consumption
- reversible causes of anaemia

ANTICOAGULANT DECISION PATHWAY
NON-VALVULAR ATRIAL FIBRILLATION / ATRIAL FLUTTER



KEY PRESCRIBING INFORMATION

SHARED DECISION MAKING

When discussing the benefits and risks of anticoagulation use clinical risk profiles and personal preferences to guide treatment choices. Discuss with the person that:

- for most people the benefit of anticoagulation outweighs the bleeding risk
- for people with an increased risk of bleeding, the benefit of anticoagulation may not always outweigh the bleeding risk, and careful monitoring of bleeding risk is important.

A variety of patient information leaflets are available to help individuals with decision making. The Atrial Fibrillation Association has several booklets which are available to download – https://www.heartrhythmalliance.org/afa/uk/anticoagulation-af-related-stroke-prevention

ANTIPLATELETS

Do not offer aspirin monotherapy solely for stroke prevention to people with NVAF
For guidance on antiplatelet therapy for people who have had a myocardial infarction and are having anticoagulation, see antiplatelet therapy for people with an ongoing separate indication for anticoagulation in NICE's guideline on acute coronary syndromes.

REVIEW OF PATIENTS WITH NON-VALVULAR ATRIAL FIBRILATION

For people who are not taking an anticoagulant, review stroke risk when they reach age 65 or if they develop any of the following at any age:

- diabetes
- heart failure
- peripheral arterial disease
- coronary heart disease
- stroke, transient ischaemic attack or systemic thromboembolism.

For people who are not taking an anticoagulant because of bleeding risk or other factors, review stroke and bleeding risks annually, and ensure that all reviews and decisions are documented.

For people who are taking an anticoagulant, review the need for anticoagulation and the quality of anticoagulation at least annually, or more frequently if clinically relevant events occur affecting anticoagulation or bleeding risk.

Assess anticoagulation control in people taking VKAs at each review and anticoagulant monitoring appointment. Calculate TTR and reassess appropriateness of VKA based on results.

SWITCHING FROM WARFARIN TO A DOAC

Switching appropriate patients from warfarin to a DOAC may be considered to avoid regular blood tests for INR monitoring. Whilst DOACs require blood tests to assess renal function throughout treatment, the monitoring is predictable, less rigorous than INR testing with warfarin and is routinely carried out in primary care.

Switching from warfarin to a DOAC must be done with careful consideration as not all patients are suitable for a switch to a DOAC, and in some cases, specialist advice may be required. Patients should only be switched from warfarin to a DOAC by clinicians in primary or secondary care with experience in managing anticoagulation. Use warfarin in patients with mechanical heart valves (metallic), moderate to severe mitral stenosis and in antiphospholipid syndrome.

See Guidance for the Safe Switching of Warfarin to Direct Oral Anticoagulants (DOACs) for Patients with Non-Valvular AF and Venous Thromboembolism (DVT / PE) for further information and guidance.

PATIENT COUNSELLING CHECKLIST FOR ANTICOAGULATION IN NVAF

	COUNSELLING POINT	YES / NO
1.	Explanation of an anticoagulant (increases clotting time and reduces risk of clot formation) Explanation of indication for therapy (NVAF and stroke risk)	
2.	Differences between DOACs and warfarin *(for patients converting from warfarin to DOAC therapy or offering choice of anticoagulation agent)* • No routine INR monitoring • Fixed dosing • No dietary restrictions and alcohol intake permitted (within national guidelines) • Fewer drug interactions	
3.	Discuss bleeding risk & ensure shared decision making on the choice of anticoagulant. The rationale for the use of the chosen anticoagulant has been discussed and explained, and patient agrees	
4.	Duration of therapy has been discussed (lifelong) Female patients – If pregnant or breast-feeding, or planning pregnancy, speak to clinician	
5.	Patient has been made aware of the importance of always carrying an anticoagulant Patient Alert Card. The patient understands they must inform healthcare professionals, including doctors, pharmacists and dentists that they are taking an oral anticoagulant and to show their Patient Alert card. Alert cards should be provided by community pharmacies. Also available to order from the AHSN. Individual alert cards are also available to download below: Apixaban Rivaroxaban Dabigatran Edoxaban Warfarin **If initiating warfarin, the patient should be supplied with a yellow Warfarin Anticoagulant Record book.**	
6.	A medication specific patient information leaflet has been given to the patient Apixaban Rivaroxaban Dabigatran Edoxaban Warfarin	
7.	The patient knows how to take the medication including: • The dose • The frequency of administration • Timing – aim to take at the same time(s) each day. If twice daily preparation then aim for 12 hours between doses. • Take with water, with or without food (Rivaroxaban must be taken with food)	
8.	The patient understands the importance of adherence • Loss of effectiveness if poorly compliant – DOAC drug levels falls rapidly • Ways to remember to take medication e.g. reminder on phone • Do not to stop taking medication unless advised to do so by a clinician	
9.	The patient knows what to do if a dose is missed (see FAQs)	
10.	The patient knows what to do if an extra dose is taken – Contact GP/Pharmacist/NHS 111 for advice immediately	
11.	The potential side effects have been explained including when to seek medical attention. Edoxaban only – no known reversal agent but this should not be a barrier to taking	
12.	Follow-up appointments, blood tests, and repeat prescriptions: where and when has been explained.	
13.	The patient is aware of potential drug interactions • Avoid over the counter medicines containing aspirin (e.g. flu remedies), NSAIDs (e.g. ibuprofen, naproxen, diclofenac) or herbal products. Paracetamol is the preferred analgesic. • Patient to inform clinician of any new medications • Excess alcohol consumption not advised due to risks of alcohol associated acute injuries, chronic liver disease and higher risk of GI bleeding.	
14.	The patient is aware of the storage requirements: • Dabigatran must be kept in original packaging – moisture sensitive. • All other DOAC are suitable for standard medication compliance aids/ dosette boxes if required • Warfarin – not usually suitable for a dosette due to frequently changing dose	
15.	The patient has been given the opportunity to ask questions	

WARNINGS & PRECAUTIONS FOR USE

	DOACs				VKA
	APIXABAN	**RIVAROXABAN**	**DABIGATRAN**	**EDOXABAN**	**WARFARIN**
Contra-indications	• Hepatic disease associated with coagulopathy and clinically relevant bleeding risk • Active clinically significant bleeding • Concomitant treatment with any other anticoagulant agent • Lesion or condition considered significant risk factor for major bleeding*	• Pregnancy and breast-feeding • Hepatic disease associated with coagulopathy and clinically relevant bleeding risk including cirrhotic patients with Child Pugh B and C • Active clinically significant bleeding • Concomitant treatment with any other anticoagulants • Lesion or condition, if considered to be a significant risk for major bleeding*	• Patients with severe renal impairment (CrCL < 30 mL/min) • Hepatic impairment or liver disease expected to have any impact on survival • Concomitant treatment with strong P-gp inhibitors • Prosthetic heart valves requiring anticoagulant treatment • Active clinically significant bleeding • Concomitant treatment with any other anticoagulants • Lesion or condition, if considered a significant risk factor for major bleeding*	• Pregnancy and breast-feeding • Hepatic disease associated with coagulopathy and clinically relevant bleeding risk. • Uncontrolled severe hypertension. • Clinically significant active bleeding. • Concomitant treatment with any other anticoagulants • Lesion or condition, if considered to be a significant risk for major bleeding*	• Haemorrhagic stroke • Clinically significant active bleeding • Within 72 hours of major surgery with risk of severe bleeding • Within 48 hours postpartum • Pregnancy (first and third trimesters) • Drugs where interactions may lead to a significantly increased risk of bleeding • Lesion or condition, if considered to be a significant risk for major bleeding*
	* May include current or recent gastrointestinal ulceration, presence of malignant neoplasms at high risk of bleeding, recent brain or spinal injury, recent brain, spinal or ophthalmic surgery, recent intracranial haemorrhage, known or suspected oesophageal varices, arteriovenous malformations, vascular aneurysms or major intraspinal or intracerebral vascular abnormalities.				
Use not recommended	• If CrCL <15mL/min or dialysis • In pregnancy & breastfeeding • In patients receiving concomitant systemic treatment with strong inhibitors of both CYP3A4 and P-gp	• If CrCL <15mL/min • In patients receiving concomitant systemic treatment with azole-antimycotics	• Dabigatran is not stable in compliance aids. • During pregnancy unless clearly necessary.	• If CrCL <15mL/min or dialysis • Chronic use of NSAIDs with edoxaban	• Please see SPC for drug and food interactions, including herbal products and alcohol consumption • In women of child-bearing age unless taking regular effective contraception
	• In patients with a history of thrombosis who are diagnosed with antiphospholipid syndrome • For patients with a history of poor medication adherence (unless related to difficulty in managing a variable warfarin regimen)				
Cautions	• In patients with mild or moderate hepatic impairment (Child Pugh A or B). • If CrCL 15 - 29mL/min	• If CrCL 15 - 29mL/min	• If CrCl 30-50mL/min •	• In patients with mild to moderate hepatic impairment .	• In patients with active peptic ulcers • Concomitant anti-platelet drugs
	• In patients with an increased risk of haemorrhage				

DOSING & RENAL FUNCTION

	DOACs				VKA
	APIXABAN	**RIVAROXABAN**	**DABIGATRAN**	**EDOXABAN**	**WARFARIN**
	Please see Appendix 1 – Quick reference guide for dose adjustments of DOACS in NVAF				
CrCl >50 mL/min	5mg twice daily Reduce to 2.5mg twice a day in patients with two or more of the following: • Age ≥ 80 years • Body weight ≤ 60kg • Serum creatinine ≥ 1.5mg/dL (133 mmol/L)	20mg once daily	150mg twice daily if aged <75 years 110-150mg twice daily if aged 75-80 years or increased risk of bleeding (Individual assessment of the thromboembolic risk and the risk of bleeding) 110mg twice daily if aged ≥ 80 years or concomitant Verapamil	60mg once daily *N.B. There is a trend towards decreasing efficacy with increasing CrCl, therefore only use in patients with high CrCl after evaluation of the individual thromboembolic and bleeding risk.* Reduce to 30mg once daily in patients with one or more of the following: • Body weight ≤ 60kg • Concomitant use of ciclosporin, dronedarone, erythromycin, or ketoconazole	Dose as per INR
CrCl 30-49 mL/min		15mg once daily	110-150mg twice daily	30mg once daily	Use with caution
CrCl 15-29 mL/min	2.5mg twice a day	15mg once daily (caution)	Contraindicated		
CrCl < 15mL/min	Not recommended	Not recommended		Not recommended	Caution – frequent INRs
Missed Doses	Take as soon as remembered unless it is < 6 hours before the next dose. If so, skip missed dose and take the next scheduled dose as usual.	Take as soon as remembered if it is still > 12 hours before next scheduled dose. If < 12 hours, skip missed dose and take next scheduled dose as usual.	Take as soon as remembered unless it is < 6 hours before the next dose. If so, skip missed dose and take the next scheduled dose as usual.	Take as soon as remembered. Never take more than 1 dose in a day.	If usually taken in the evening and it is before midnight on the same day, take the missed dose. If midnight has passed do not take that dose. Inform usual anticoagulation monitoring service.
	NEVER take double the prescribed dose on the same day to make up for a missed dose				
Extra Doses	Skip next scheduled dose and take the following dose the next day as usual	Contact NHS 111 for advice	Skip next scheduled dose and take the following dose the next day as usual	Contact NHS 111 for advice	Contact usual anticoagulation service or NHS 111 for advice
	If unsure, contact NHS 111 for advice, skipped doses alone might not always be suitable. Active monitoring +/- reversal might be required based on individual patient risk factors and thrombosis risk. In the case of significant active bleeding, treat as an emergency.				

Please note, CrCl should be used to calculate renal function as per MHRA advice. eGFR should **NOT** be used.
Creatinine clearance calculator available: https://www.mdcalc.com/creatinine-clearance-cockcroft-gault-equation

MONITORING & COMPLIANCE

<table>
<tr><th rowspan="2"></th><th colspan="4">DOACs</th><th>VKA</th></tr>
<tr><th>APIXABAN</th><th>RIVAROXABAN</th><th>DABIGATRAN</th><th>EDOXABAN</th><th>WARFARIN</th></tr>
<tr><td>Baseline Monitoring</td><td colspan="4">• U&Es
• CrCl
• LFTs
• FBC
• Coagulation screen
• Weight
• Blood pressure

Monitoring until patient is stabilised, ideally review every 3 months to:
• Assess compliance and reinforce advice regarding regular dosing schedule
• Enquire about adverse effects such as bleeding
• Assess for the presence of thromboembolic events
• Enquire about other medicines, including OTC medicines</td><td>• U&Es
• LFTs
• Coagulation screen
• Blood pressure</td></tr>
<tr><td>Routine Monitoring</td><td colspan="4">U&Es, LFTs & FBC

• If <75 years and CrCl >60mL/min ensure annual U&Es
• If >75 years or CrCl 30-60mL/min ensure 6 monthly U&Es
• If CrCl 15-30mL/min ensure 3 monthly U&Es
• Recalculate CrCl if any significant changes or if intercurrent condition that may have impact on renal function
NB. If CrCl <60 mL/minute, the frequency of monitoring (in months) can be guided by the CrCl divided by 10. For example, every 3 months if CrCl is 30 mL/minute. (NICE)</td><td>INR should be checked at least every 12 weeks once stable in individual therapeutic range.
If changes to patient's health or medications check more frequently.</td></tr>
<tr><td rowspan="2">Compliance Considerations</td><td>Twice daily dosing</td><td>Once daily dosing with food</td><td>Twice daily dosing
Not suitable for compliance aids</td><td>Once daily dosing</td><td rowspan="2">Variable dosing as per INR

Patients who forget doses may benefit from warfarin due to longer blood thinning effect and reminders from anticoagulation management services</td></tr>
<tr><td colspan="4">Shorter half-life compared to warfarin, erratic compliance could result in worse anticoagulation</td></tr>
<tr><td>Lactose & Wheat Content</td><td>Lactose
No wheat</td><td>Lactose
No wheat</td><td>No Lactose
No wheat</td><td>No lactose
No wheat</td><td>Lactose
Maize starch</td></tr>
</table>

SAFETY & BLEEDING RISK

	DOACs				VKA
	APIXABAN	**RIVAROXABAN**	**DABIGATRAN**	**EDOXABAN**	**WARFARIN**
Bleeding Risk	• Major bleeding: less common with apixaban than warfarin (p<0.001) • GI bleeding: no difference between apixaban and warfarin • Intracranial bleeding: less common with apixaban than warfarin (p<0.001)	• Major bleeding: no difference between rivaroxaban and warfarin • GI bleeding: more common with rivaroxaban than warfarin (p<0.001) • Approximately 88% of major bleeding episodes associated with rivaroxaban originate in GI tract • Intracranial bleeding: less common with rivaroxaban than warfarin (p=0.02)	• Major bleeding: no difference between dabigatran 150mg BD and warfarin. Less common with dabigatran 110mg BD than warfarin • GI bleeding: more common with dabigatran 150mg BD than warfarin (p=0.0008). No difference between dabigatran 110mg BD and warfarin. • Intracranial bleeding: less common with both doses of dabigatran than with warfarin (p<0.001) • Bleeding risk: high in frail/ elderly particularly with renal impairment and low weight	• Major bleeding: significantly reduced rate of major bleeding and of several secondary bleeding enpoints for 60mg/30mg edoxaban compared to warfarin (p≤0.01). • Major GI bleeding: occurred slightly more frequently in edoxaban 60mg/30mg than in warfarin (p=0.03). • In clinical studies mucosal bleedings and anaemia were seen more frequently during long term Edoxaban treatment compared with VKA treatment, therefore in addition to adequate clinical surveillance, laboratory testing of haemoglobin / haematocrit could be of value to detect occult bleeding.	• See respective agent for comparison • N.B. Falls are not a contraindication to the use of warfarin. Analytical models estimate that elderly patients would need to fall 295 times a year for their risk of developing subdural haematomas to outweigh the benefit of being anticoagulated with warfarin • Long term safety data based on over 50 years use and anticoagulant effects can be rapidly reversed in the event of major bleeding
Reversal Agents	Ondexxya▼ andexanet alfa – in life-threatening or uncontrolled bleeding in adults, only if: • The bleed is in the gastrointestinal tract • The company provides andexanet alfa according to the commercial agreement (product has conditional marketing authorization) NICE TA697		Praxbind▼, idarucizumab Dabigatran can be re-started 24 hours after administration of idarucizumab.	Currently no specific authorised reversal agent	Treatment with Vitamin K
Half-Life	12 hours	5-9 hours in young individuals 11-13 hours in the elderly	GFR ≥ 80 approx. 13 hrs GFR ≥ 50-< 80 approx. 15 hrs GFR ≥ 30-< 50 approx. 18 hrs	10-14 hours	Approx. 40 hours

SWITCHING ANTICOAGULANTS

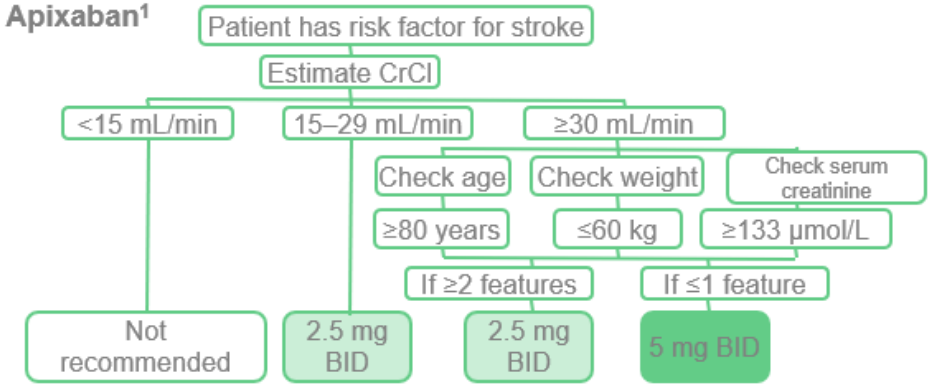
	DOACs				VKA
	APIXABAN	**RIVAROXABAN**	**DABIGATRAN**	**EDOXABAN**	**WARFARIN**
There is a potential for inadequate anticoagulation during the transition between DOACs and warfarin. Continuous adequate anticoagulation should be ensured during any transition to an alternative anticoagulant.	• When converting from apixaban to warfarin, continue apixaban for at least 2 days after starting warfarin therapy. • After 2 days of co-administration of apixaban and warfarin, obtain an INR prior to the next scheduled dose of apixaban. • Continue co-administration of apixaban and warfarin until the INR is 2 or more	• When converting from rivaroxaban to warfarin, rivaroxaban should be continued until the INR is ≥ 2.0. • For the first two days of the conversion period, standard initial dosing of warfarin should be used followed by warfarin dosing guided by INR testing. • While patients are on both rivaroxaban and warfarin, the INR should not be tested earlier than 24 hours after the previous dose but prior to the next dose of rivaroxaban. Once rivaroxaban is discontinued INR testing may be done reliably at least 24 hours after the last dose • Rivaroxaban can contribute to an elevated INR	• When converting from dabigatran to warfarin, adjust the starting time of warfarin based on creatinine clearance as follows: • For CrCl >50 mL/min, start warfarin 3 days before discontinuing dabigatran. • For CrCl 30-50 mL/min, start warfarin 2 days before discontinuing dabigatran. • For CrCl 15-30 mL/min, start warfarin 1 day before discontinuing dabigatran • For CrCl <15 mL/min, no recommendations can be made – consult with haematologist. • Because dabigatran can contribute to an elevated INR, the INR will better reflect warfarin's effect after dabigatran has been stopped for at least 2 days.	• When converting from edoxaban to warfarin, continue edoxaban until the INR is ≥ 2.0. • A loading dose of warfarin is not recommended. • Administer half of usual Edoxaban dose alongside VKA i.e. for patients currently on 60mg daily, administer 30mg. And for patients currently on 30mg daily, administer 15mg daily. • During the first 14 days of concomitant therapy measure the INR at least 3 times, just prior to the daily dose of edoxaban • Edoxaban can contribute to an elevated INR.	When converting patients from warfarin therapy to a DOAC, discontinue warfarin and start: • Apixaban and Dabigatran when INR is < 2.0 • Edoxaban when INR is < 2.5 • Rivaroxaban when INR is < 3 EHRA guidance gives pragmatic guidance on when to start DOACs after stopping warfarin: • If INR < 2: Commence DOAC that day • If INR between 2 and 2.5: Commence DOAC the next day (ideally) or the same day • If INR between 2.5 and 3: Withhold warfarin for 24-48 hours and then initiate DOAC

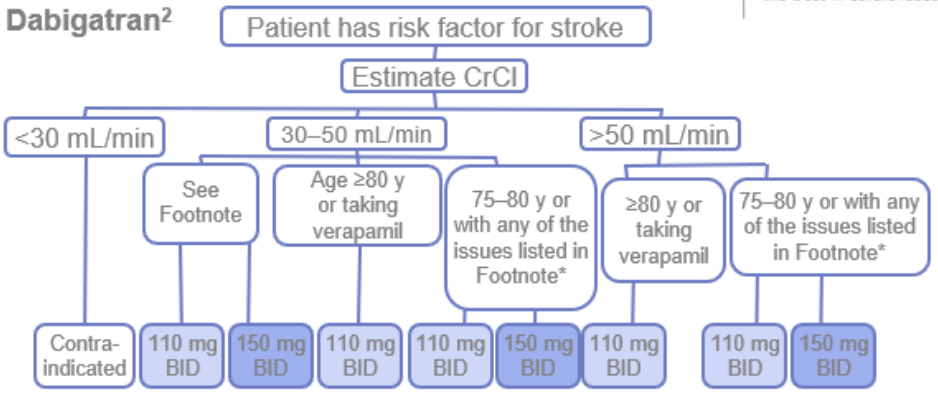
APPENDIX 1 – QUICK REFERENCE GUIDE FOR DOSE ADJUSTMENTS OF DOACS IN NVAF

Dose adjustments of DOACs for patients with NVAF

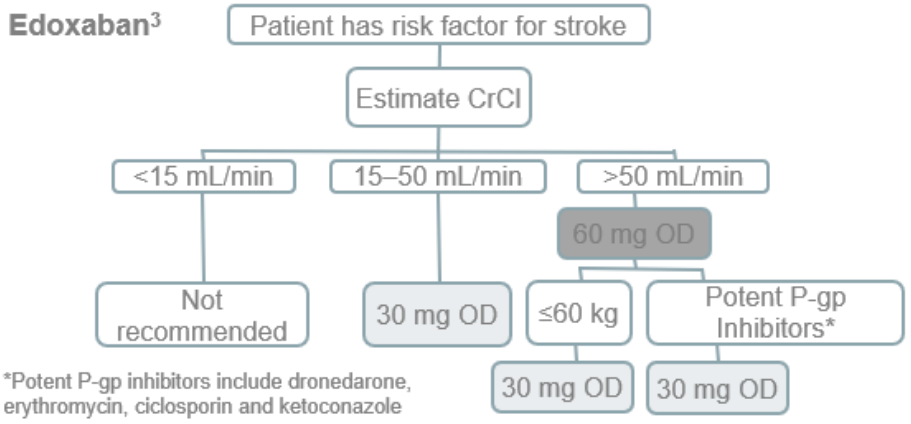
Primary Care Cardiovascular Society

Driving primary care to deliver the best in cardiovascular health

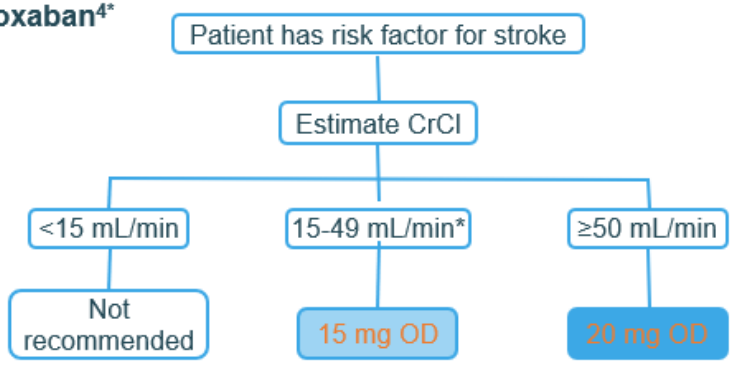




*Dabigatran dose of 110 mg or 150 mg BID, based on individual assessment of thromboembolic and bleeding risk in patients with gastritis, esophagitis or gastroesophageal reflux, or increased bleeding risk



*Potent P-gp inhibitors include dronedarone, erythromycin, ciclosporin and ketoconazole



*Rivaroxaban to be used with caution in patients with CrCl 15–29 mL/min, and in patients with renal impairment concomitantly receiving other medicinal products that increase rivaroxaban plasma concentrations.

BID, twice daily; CrCl, creatinine clearance; OD, once daily.

1. Apixaban SmPC; 2. Dabigatran SmPC; 3. Edoxaban SmPC; 4. Rivaroxaban SmPC.

REFERENCES

BNF Oral Anticoagulants https://bnf.nice.org.uk/treatment-summary/oral-anticoagulants.html

County Durham & Tees Primary Care Suggested Drug Monitoring Recommendations (March 2021) https://medicines.necsu.nhs.uk/download/drug-monitoring-recommendations/

NICE Clinical Guideline NG196: Atrial Fibrillation: Diagnosis Management (June 2021) https://www.nice.org.uk/guidance/ng196/resources/atrial-fibrillation-diagnosis-and-management-pdf-66142085507269

NICE CKS Anticoagulation – Oral: Management (August 2021) https://cks.nice.org.uk/topics/anticoagulation-oral/management

MHRA Direct-acting oral anticoagulants (DOACs): Reminder of bleeding risk, including availability of reversal agents (June 2020)
https://www.gov.uk/drug-safety-update/direct-acting-oral-anticoagulants-doacs-reminder-of-bleeding-risk-including-availability-of-reversal-agents

MHRA Prescribing Medicines in Renal Impairment: Using the Appropriate Estimate of Renal Function to Avoid the Risks of Adverse Drug Reactions (October 2019) https://www.gov.uk/drug-safety-update/prescribing-medicines-in-renal-impairment-using-the-appropriate-estimate-of-renal-function-to-avoid-the-risk-of-adverse-drug-reactions

SPC Eliquis 5mg Film-Coated Tablets https://www.medicines.org.uk/emc/product/2878/smpc

SPC Xarelto 15mg & 30mg Film-Coated Tablets https://www.medicines.org.uk/emc/product/8419/smpc

SPC Pradaxa 110mg Hard Capsules https://www.medicines.org.uk/emc/product/6229/smpc

SPC Lixiana 60mg Film-Coated Tablets https://www.medicines.org.uk/emc/product/6905/smpc

SPC Warfarin 0.5mg Tablets https://www.medicines.org.uk/emc/product/2803/smpc

The 2021 European Heart Rhythm Association Practical Guide on the Use of Non-Vitamin K Antagonist Oral Anticoagulants in Patients with Atrial Fibrillation (April 2021) https://academic.oup.com/europace/article/23/10/1612/6247378