

Frequently asked questions (FAQs) concerning Direct Acting Oral Anticoagulants (DOACs) for primary care practitioners in South West London

This guidance has been written by anticoagulation specialists in South London in answer to common questions received by anticoagulation teams and medicines optimisation teams in South West London from healthcare practitioners (HCPs) concerning patients taking DOACs.

The aim of this guidance is to provide information to assist HCPs with queries concerning DOACs and advice concerning when a referral and/or further investigation is appropriate for their patient.

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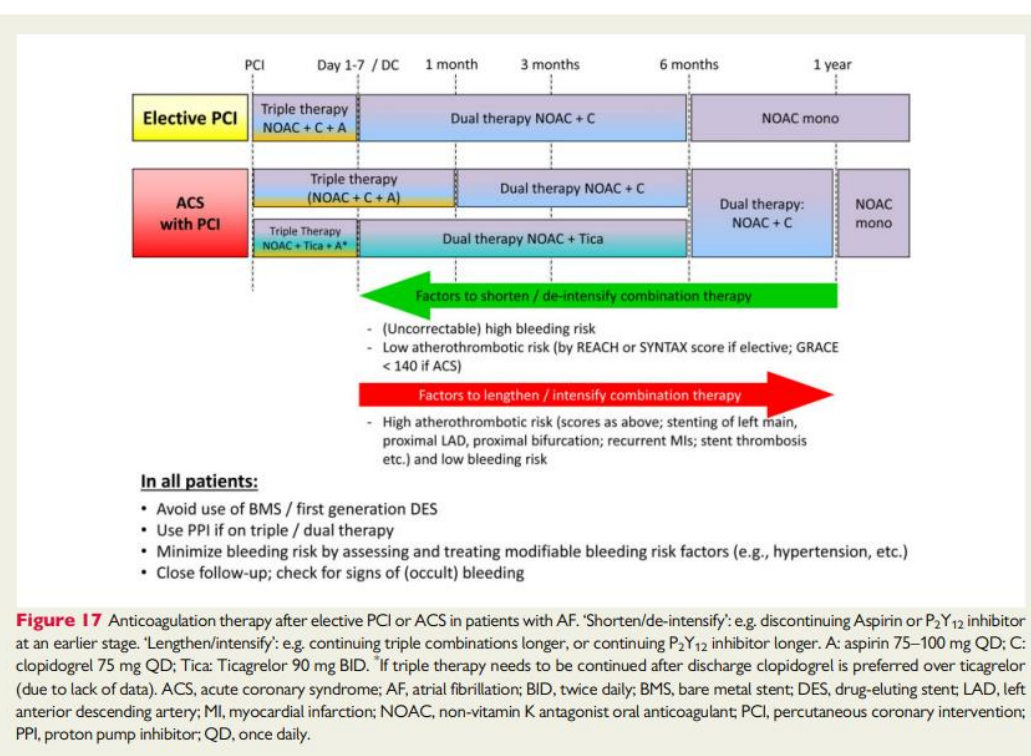
Question:	Answer:
1.How should patients at higher risk of bleeding be monitored?	There is no standard approach. It depends on the bleeding risk and clinical circumstances. Patients should be counselled to monitor for signs of bleeding and to report to their general practitioner (GP) or emergency department (ED) as appropriate.

	This advice is the same as for warfarin patients although it should be noted that the risk of major bleeding, particularly intracranial haemorrhage, is significantly reduced with DOACs.																				
2. What to do if haemoglobin (Hb) drops?	If Hb <100g/L or change from baseline >20g/L, investigate for cause and consider referral to/review by a specialist based on initial investigations. Referral will depend on the suspected underlying cause: – <ol style="list-style-type: none"> 1) If GI bleeding/cancer will need referral to gastroenterology/colorectal 2) If menorrhagia is not controlled with measures offered, consider a gynaecology referral +/-haematology advice re. choice of anticoagulant. 3) For haematuria – urology referral +/- haematology advice if ongoing bleeding is an issue The relevant specialist may not always be a haematologist. Depending on clinical context and degree of Hb drop, consider stopping anticoagulation and investigate for cause of Hb drop or low Hb as necessary, and in line with NICE recommendations for cancer investigations. Stopping anticoagulation may be temporary while investigations occur.																				
3. Calculating renal function (creatinine clearance)	<p>Use recent results:</p> <ul style="list-style-type: none"> • Blood results from within the last month • Body weight from within the last year (unless significant change) <p>Calculation method:</p> <ul style="list-style-type: none"> • Use actual body weight for Cockcroft-Gault formula • Do NOT use eGFR (it can overestimate renal clearance, especially in elderly or low body weight patients) <p>Tools:</p> <ul style="list-style-type: none"> • Recommended calculator: https://www.mdcalc.com/creatinine-clearance-cockcroft-gault-equation <p>Specialist advice required for:</p> <ul style="list-style-type: none"> • Extremes of body weight (<50 kg or >120 kg) • Dialysis patients CrCl <15 mL/min (DOACs contraindicated) • Heart failure with fluid overload (use dry weight) • Patients with amputations or severe muscle loss 																				
4. What to do if renal function (creatinine clearance) is impaired?	Adjust DOAC dose as per summary of product characteristics (SPC) for the DOAC agent (via www.medicines.org.uk): (see <i>DOAC initiation/monitoring template</i>): <table border="1" data-bbox="411 1491 1445 1984"> <thead> <tr> <th>SPC hyperlinks:</th> <th>Apixaban</th> <th>Rivaroxaban</th> <th>Dabigatran</th> <th>Edoxaban</th> </tr> </thead> <tbody> <tr> <td>Standard dose</td> <td>5mg BD</td> <td>20mg OD (with food)</td> <td>150mg BD</td> <td>60mg OD</td> </tr> <tr> <td>Reduced dose</td> <td>2.5mg BD</td> <td>15mg OD (with food)</td> <td>110mg BD</td> <td>30mg OD</td> </tr> <tr> <td>Criteria for reduced dose</td> <td> ≥ 2 of; <ul style="list-style-type: none"> • Age ≥ 80yrs • weight ≤ 60kg • Cr ≥ 133µmol/L OR CrCl 15-29ml/min </td> <td>CrCl 15 to 49ml/min</td> <td> <ul style="list-style-type: none"> • Age ≥ 80 yrs • On verapamil • Consider for: <ul style="list-style-type: none"> ○ Reflux/gastritis ○ Age 75-80 yrs ○ CrCl 30-50ml/min ○ “Bleed risk” </td> <td> ≥ 1 of <ul style="list-style-type: none"> • weight ≤ 60kg • CrCl 15-50ml/min • On ciclosporin, dronedarone, erythromycin, ketoconazole </td> </tr> </tbody> </table>	SPC hyperlinks:	Apixaban	Rivaroxaban	Dabigatran	Edoxaban	Standard dose	5mg BD	20mg OD (with food)	150mg BD	60mg OD	Reduced dose	2.5mg BD	15mg OD (with food)	110mg BD	30mg OD	Criteria for reduced dose	≥ 2 of; <ul style="list-style-type: none"> • Age ≥ 80yrs • weight ≤ 60kg • Cr ≥ 133µmol/L OR CrCl 15-29ml/min	CrCl 15 to 49ml/min	<ul style="list-style-type: none"> • Age ≥ 80 yrs • On verapamil • Consider for: <ul style="list-style-type: none"> ○ Reflux/gastritis ○ Age 75-80 yrs ○ CrCl 30-50ml/min ○ “Bleed risk” 	≥ 1 of <ul style="list-style-type: none"> • weight ≤ 60kg • CrCl 15-50ml/min • On ciclosporin, dronedarone, erythromycin, ketoconazole
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	Contra-indicated	CrCl <15ml/min	CrCl <15ml/min	CrCl <30ml/min	CrCl <15ml/min (caution CrCl >95ml/min)																																					
	<p>Continue to monitor the patient with the frequency dictated by the SWL DOAC Initiation Guidance, including at least 4 monthly monitoring for elderly DOAC patients aged over 75 years and frail patients</p> <p>If CrCl is <15ml/min (<30ml/min for dabigatran) DOACs are contra-indicated-stop DOAC and refer back to anticoagulation for urgent switch to warfarin.</p> <p>Dialysis patients –discuss with the renal team regarding suitability for anticoagulation. The risk/benefit profile of anticoagulation in AF for dialysis patients is not clear.</p>																																									
5. What to do if platelets drop?	<p>Any platelet count below 100 should be monitored closely and investigated further:</p> <p>If platelet count is 50-75: monitor closely (at least monthly) and advise patient to report any bleeding. Refer to local haematology clinic for further investigation as appropriate.</p> <p>If platelets <50 – advise patient to stop taking anticoagulant and seek advice from local anticoagulation/haematology team.</p>																																									
6. What to do if liver function changes?	<p>If liver transaminases: AST or ALT >2 x upper limit of normal (ULN) or bilirubin >1.5 x ULN, or if liver disease is associated with clinically relevant bleeding risk e.g. presence of varices – discuss with local anticoagulation clinic.</p>																																									
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Advice will be given to primary care from the pre-assessment clinic- seek further advice from surgical or haematology team, or initiating clinician/dentist if this is unclear.													
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The DOAC will be restarted by the hospital surgical team or anticoagulation clinic post-operatively and/or bridged with LMWH (eg dalteparin or enoxaparin) as necessary.													
8. How should frail patients at high falls risk be managed?	For these patients no dose reduction is required. A study by <i>Man-Son-Hing et al Arch Intern Med. 1999;159:677-685</i> showed a patient would have to fall >295 times/year for the risks associated with warfarin therapy to outweigh the benefit. This data can be extrapolated to the DOAC population. If you have concerns about a cerebral bleed risk or would like further advice please refer to the local falls clinic or haematologist. Renal function, liver function and haemoglobin for frail patients should be monitored every 4 months regardless of age.												
9. When should antiplatelets be reviewed in combination with oral anticoagulation (OAC)?	When starting a patient on a DOAC, if they are already on an antiplatelet, the indication for the antiplatelet should be established. If the antiplatelet is prescribed for any indication other than for secondary prevention of cardiovascular events or peripheral vascular disease, then it can usually be stopped. For secondary prevention, the time of the last cardiovascular event should be established - if it was more than one year ago then the antiplatelet can usually be stopped. However, if these patients are under the care of a cardiologist, stroke or vascular specialist, they should be consulted as												

balancing the clinical need for anticoagulant and antiplatelets is often a complex decision based on more than one factor (refer to SWL antiplatelet guidance- update under review)



The table above provides a guide as to how triple therapy should be managed for cardiology indications and the durations you may expect to see, reference:

[2021 European Heart Rhythm Association Practical Guide on the Use of Non-Vitamin K Antagonist Oral Anticoagulants in Patients with Atrial Fibrillation | EP Europace | Oxford Academic](#)

There is no standardised approach for patients with cerebrovascular or vascular indications for antiplatelets.

10. Can patients being investigated for cancer be treated with DOACs?

For a new presentation of an unprovoked venous thromboembolism (VTE) to secondary care, patients will be started on low molecular weight heparin (LMWH) over a DOAC whilst they undergoing urgent (2 week wait) investigations. Only if the results are negative, or under specialist haematology guidance, would the patient be switched to a DOAC.

If a patient is undergoing investigations for cancer when already established on a DOAC, the DOAC should be continued unless the patient has presented with bleeding (the risk of bleeding verses the risk of stroke should be weighed up in this instance). The oncologist or haematologist investigating the cancer should be reviewing the choice of anticoagulant and switching to LMWH if appropriate. If you do not think that the anticoagulant has been considered, please contact them for advice.

See [13. Can DOACs be prescribed in patients with malignancy?](#) for more information on confirmed cancer diagnosis.

<p>11. What if my patient has haematuria?</p>	<p>Patients taking DOACs are managed by the same pathway as when haematuria is investigated or managed in general practice. Whilst it is a listed side effect of all DOACs, the cause of the haematuria should still be fully investigated. It would be prudent to also check full blood count (FBC), urea and electrolytes (U+Es) and renal profile (CrCl).</p> <p>The DOAC should be continued whilst awaiting investigations where possible, after assessing the risk of stroke against the risk of bleeding (involving the patient in this discussion). Where a patient has significant haematuria that is ongoing, or a Hb drop where this is the likely source, withholding the DOAC (temporarily while this is investigated) may be appropriate.</p> <p>Consider the patient's HASBLED/ORBIT score and modifiable risk factors for bleeding, as these should be optimised/minimised when prescribing DOACs.</p>
<p>12. Nosebleed and other minor / nuisance bleeding?</p>	<p>In general, patients should be counselled on DOAC initiation and at every review that, should nuisance and minor bleeding occur, to continue the DOAC unless otherwise advised by a healthcare professional.</p> <p>It would be prudent to check FBC, LFTs and Renal Profile on presentation.</p> <p>Nose Bleeds:</p> <p>Patients should be advised to practice first aid (as outlined here:- https://cks.nice.org.uk/epistaxis-nosebleeds) should a nosebleed occur. If the nosebleed does not stop after 10-15 minutes of nasal pressure, they should attend A+E. It is likely that the patient will be advised to miss one dose of the DOAC.</p> <p>If first aid measures result in the cessation of bleeding within 10-15 minutes the patient does <u>not</u> need to attend A+E or miss any doses of DOAC.</p> <p>In all instances, the patient should be advised to avoid activities that increase the risk of re-bleeding for 24 hours e.g. blowing the nose or heavy lifting.</p> <p>If nose bleeds are recurrent, ask the patient to record how often these are occurring, for how long, and if they have missed any doses of the DOAC. Assess the cause of the nose bleeds (as outlined here: https://cks.nice.org.uk/epistaxis-nosebleeds#!scenarioRecommendation:1) and, if needed, prescribe topical treatment with an antiseptic preparation. In some circumstances an ENT referral may be required.</p> <p>Bleeding Gums:</p> <p>Bleeding gums usually occur when brushing teeth or flossing. Patients should be advised not to miss any doses of the DOAC and that bleeding gums are a harmless side effect. The most likely cause is plaque-induced gingival inflammation and hence patients should be advised to follow good oral hygiene and attend for regular check-ups at the dentist.</p> <p>Should the bleeding gums be excessive or prolonged, refer the patient to the dentist / periodontist for a through dental examination.</p>
<p>13. Can DOACs be prescribed in patients with malignancy?</p>	<p>AF treatment:</p> <p>Little evidence for this cohort. Ideally keep on current anticoagulant (DOAC or warfarin)</p> <p>Consider drug-drug interactions (with chemotherapy) and creatinine clearance (CrCl).</p> <p>Consider bleeding risk and thrombosis risk (cancer not a factor in either HASBLED or CHA₂DS₂VASc) and patient wishes if de-prescribing anticoagulation.</p>

	<p>VTE treatment: Evidence to show can use DOACs in active cancer patients. Low-molecular weight heparins (LMWHs) are preferred for patients with gastrointestinal malignancies or high risk of bleeding. <i>Hokusai VTE Cancer study 2018</i></p> <ul style="list-style-type: none"> • Edoxaban vs. dalteparin • Edoxaban was non-inferior to dalteparin for the combined outcome of recurrent thrombosis and major bleeding. <p><i>SELECT-D trial 2018</i></p> <ul style="list-style-type: none"> • Rivaroxaban vs. dalteparin in patients with cancer • Rivaroxaban was associated with a lower risk of recurrent VTE <p><i>APIXABAN</i></p> <ul style="list-style-type: none"> • Apixaban for the Treatment of Venous Thromboembolism Associated with Cancer • Extended Reduced-Dose Apixaban for Cancer-Associated Venous Thromboembolism
<p>14. Is there an antidote for DOACs?</p>	<p>Outcomes of major bleeds with DOACs are no worse than those with warfarin even in the absence of clinically available antidotes.</p> <p>There is a 50% reduction of intracerebral haemorrhage (ICH) and fatal bleeds with DOACs compared with warfarin, although the absolute reduction is limited to 2 intracranial bleeds and 1 fatal bleed per 1000 patients per year.</p> <p>Gastrointestinal haemorrhage was more frequent in patients taking DOACs than warfarin.</p> <p>DOACs have a short half-life so withholding the medication and supportive care should be utilised in all circumstances of major bleeding.</p> <p>Haematology and Emergency departments in hospital can advise on use of activated charcoal, tranexamic acid and prothrombin complex concentrates.</p> <p>There are 2 reversal agents currently available:</p> <ul style="list-style-type: none"> • Idarucizumab – for the rapid reversal of dabigatran. It may be necessary for emergency surgery/urgent procedures and in life-threatening or uncontrolled bleeding. • Andexanet alfa - for apixaban or rivaroxaban, when reversal of anticoagulation is needed due to life-threatening or uncontrolled bleeding. As per NICE, Andexanet alfa is only currently recommended where the bleed is in the gastrointestinal tract.
<p>15. What references are available for dosing queries?</p>	<p>For DOACs the dose reduction criteria varies between agents and indications.</p> <p>For the most up-to-date dosing please refer to the Summary of Product Characteristics (SPC) for each DOAC at: https://www.medicines.org.uk/emc/</p>
<p>16. How do I counsel patients? Who can I refer to?</p>	<p>There is a counselling checklist included as part of the DOAC Initiation in NVAf and DOAC Monitoring (all indications) Guidance for HCPs</p> <p>There are patient materials available to support patient education, including printed leaflets and websites:</p> <p>AF Association https://www.heartrhythmalliance.org/afa/uk/ British Heart Foundation https://www.bhf.org.uk/</p> <p>For patients with a history of venous thromboembolism: Thrombosis UK https://thrombosisuk.org/</p>

	<p>Many of the acute hospital trusts and pharmaceutical companies have their own patient information leaflets (PILs) which should be provided to patients.</p> <p>Community pharmacists and practice-based pharmacists can also help support DOAC adherence and understanding.</p> <p>For anticoagulation cards (OATALERTCARD): Supplier for GP Practices now Primary care Support England not Xerox via nhs.forms.co.uk:Email: pcse.suppliesleeds@nhs.net OR PCSE.DataManager@nhs.net OR PCSE.AdHoc-MR@nhs.net</p>
<p>17. How do I manage DOACs in obesity?</p>	<p>The International Society on Thrombosis and Haemostasis (ISTH) recommends that standard doses of rivaroxaban or apixaban are among appropriate anticoagulant options regardless of high BMI and weight. Fewer supportive data exist for apixaban than rivaroxaban. This statement relates to the use of DOACs for the treatment of VTE, though this could be equally applied to DOAC use in NVAf. However, for patients weighing >150kg, seek specialist advice from a Haematologist.</p>
<p>18. For housebound patients, how will they be weighed before initiation and for follow ups?</p>	<p>Patients will be weighed at initiation, during an inpatient stay or in outpatient clinics. Telephone initiations are only done at the clinician's discretion, and the current weight will be confirmed with the patient or in the medical records. It is recommended that patients are weighed at least annually, as part of their annual anticoagulation review in primary care, and to enable an accurate calculation of creatinine clearance (CrCl).</p>
<p>19. How do I switch to (for example) edoxaban or rivaroxaban from another DOAC? From warfarin?</p>	<p>Continued anticoagulant therapy is vitally important in patients with NVAf. According to the summary of product characteristics (SPC: www.medicines.org.uk) and NICE CKS, discontinue dabigatran or apixaban and start edoxaban or rivaroxaban at the time of the next dose of the oral anticoagulant (e.g. normally the following morning). It would be good practice to review the patient at 6 to 8 weeks after the switch to confirm that they are tolerating the change in DOAC. Patients should be advised to use up the supply of original DOAC before starting the newly prescribed edoxaban or rivaroxaban in order to negate any wastage (medication costs, dispensing costs/pharmacist time etc).</p> <p>In all cases exercise clinical judgement and ensure that, if the patient is under a specialist, that they have been consulted (eg advice and guidance), and previous correspondence has been reviewed, before switching (unless switching due to drug intolerance- report all significant suspected reactions to DOACs to the Yellow Card Scheme (www.mhra.gov.uk/yellowcard)). Speak to anticoagulation (AC) specialist pharmacists for advice if needed.</p> <p>See warfarin to DOAC switching guidance from COVID-19 pandemic, appendix 1: Microsoft Word - FINAL guidance on safe switching of warfarin to DOAC COVID-19 Mar 2020 (rpharms.com) Seek advice and guidance from your local anticoagulation clinic for patients switching from warfarin and for their follow up/monitoring requirements.</p>

<p>20. How do I find out what medicines interact with DOACs? How do I manage them?</p>	<p>Please refer to the British National Formulary (BNF) and Summary of Product Characteristics (SPC) for the DOAC agent for further details: BNF: https://bnf.nice.org.uk/interactions/ SPC: www.medicines.org.uk For HIV medications see: https://www.hiv-druginteractions.org/ Common interactions to consider are with antiepileptic agents, HIV antiretrovirals, hepatitis antivirals, antifungals and chemotherapy agents.</p> <p>Some DOACs require a dose adjustment, some require more frequent monitoring and, in some cases, should not be prescribed in combination with interacting medicines. Please consult a pharmacist for advice.</p>
<p>21. What happens if my patient develops a skin rash on a DOAC?</p>	<p>Maculopapular rashes are drug-induced in approximately 50 to 70% of adult patients, and should be a suspected cause if a skin rash begins within 4 to 12 days of starting a new medicine, although some rashes may occur later. If the timing of onset of the skin rash fitted with when the DOAC started, and there is no other cause, then try switching to an alternative DOAC to see if the rash improves. If the rash is very mild then the patient may be happy to continue for short while to see if the rash improves on the same DOAC.</p> <p>Please note: Serious skin reactions, including Stevens-Johnson syndrome/toxic epidermal necrolysis and DRESS syndrome, have been reported during post-marketing surveillance in association with the use of rivaroxaban. Patients appear to be at highest risk for these reactions early in the course of therapy: the onset of the reaction occurring in the majority of cases within the first weeks of treatment. Rivaroxaban should be discontinued at the first appearance of a severe skin rash (e.g. spreading, intense and/or blistering), or any other sign of hypersensitivity in conjunction with mucosal lesions.</p> <p>This rare reaction may also be possible with other DOAC agents (as with other medications) but have not been reported in literature.</p>
<p>22. Contact details for local anticoagulation services in SWL</p>	<p>For St Georges University Hospitals: Tel 02087255443 (<i>prefer telephone queries currently</i>) For Croydon Health Services: CUH: ch-tr.anticoag@nhs.net Tel 02084013000 ext 5673 For Croydon Integrated Community Anticoagulation Service (CICAS) ch-tr.cicas@nhs.net For Epsom and St Helier: St Helier Hospital, haematology Tel: 020 8296 2214 Epsom Hospital, haematology Tel: 01372 73 5958 For Kingston University Hospital: AC referrals khn-tr.anticoagulationservicereferrals@nhs.net Tel: 0208 934 2041 / 2053 / 2303 for Administration Office or Tel: 0208 934 2038 / 2041 for Clinical Nurse Specialist</p>

Document History

Version: **V 1.2 (formatting)**

Author: **SWL Cardiovascular Network**

Approved by: Integrated medicines optimisation committee (IMOC)

Approval date: **December 2025**

Review Date: 2 years from approval date or sooner where appropriate