

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

This guidance has been written by anticoagulation specialists in answer to common questions received by anticoagulation teams and medicines optimisation teams in South East 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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1. How should patients at higher risk of bleeding be monitored?

There is no standard approach. It depends on the bleeding risk which is assessed and modified using [HASBLED](#) and [ORBIT](#) tools for AF patients and individual 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:

- 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.

Please note: The relevant specialist may not always be a haematologist. Depending on the clinical context and degree of Hb drop, seek specialist advice when considering stopping anticoagulation and investigate for the cause of Hb drop or low Hb as necessary, and in line with NICE recommendations for cancer investigations - [suspected cancer: recognition and referral](#). Stopping anticoagulation may be temporary while investigations occur

3. What to do if renal function (creatinine clearance) is impaired?

Calculate creatinine clearance (CrCl) as per [SEL guidance](#). Adjust DOAC dose as per summary of product characteristics ([SPC](#)) for the DOAC agent and see the table below for patients with NVAf ([DOAC initiation/monitoring template](#)) :

- Using the practice recall system continue to monitor the patient with the frequency dictated by the [SEL renal monitoring \(CrCl\) guidance](#), including 4 to 6 monthly monitoring for elderly DOAC patients aged over 75 years and frail patients (EHRA)
- Consider using the [SEL IMOC](#) practice template for DOAC patient reviews
- If CrCl is <15ml/min (<30ml/min for dabigatran) DOACs are contraindicated. Stop the DOAC and refer back to anticoagulation for an urgent switch to warfarin.

	Edoxaban	Rivaroxaban	Apixaban	Dabigatran
Standard dose	60mg OD	20mg OD (with food)	5mg BD	150mg BD
Reduced dose	30mg OD	15mg OD (with food)	2.5mg BD	110mg BD
Criteria for reduced dose in NVAf indication only	1 or more of <ul style="list-style-type: none"> - Weight ≤ 60kg - CrCL 15-50ml/min - On ciclosporin, dronedarone, erythromycin, ketoconazole 	CrCL 15-49ml/min	2 or more of : <ul style="list-style-type: none"> - Age ≥ 80 years - Weight ≤ 60kg - Cr ≥ 133µmol/L OR CrCL 15- 29ml/min	<ul style="list-style-type: none"> - Age ≥ 80 years - On verapamil - Consider reduced dose for reflux/gastritis, age 75-80 yrs., CrCL 30-50ml/min, "bleed risk"
Contraindicated	CrCL ≤ 15ml/min Caution in CrCL ≥ 95ml/min	CrCL < 15ml/min	CrCL <15ml/min	CrCL <30ml/min
Compliance aid	Compatible	Compatible	Compatible	Non-compatible

- For renal dialysis patients** –discuss with the patient’s renal team regarding suitability for anticoagulation.
- The risk/benefit profile of anticoagulation in AF for dialysis patients is not clear.
- Selected dialysis patients may be started on apixaban 2.5mg bd for AF stroke prevention or VTE prevention – only to be initiated by renal or haematology teams

4. What to do if platelets drop?

Any platelet count below $100 \times 10^9/\text{L}$ should be monitored closely (quarterly) and investigated further:

If platelet count is 50 to 75: monitor closely (at least monthly) and advise patient to report any bleeding. Refer to local haematology clinic for further investigation as appropriate.

If platelets <50 – advise patient to stop taking anticoagulant and seek advice from local anticoagulation/haematology team.

5. What to do if liver function changes?

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 regarding continued suitability for anticoagulation.

Refer to liver specialists for investigation as appropriate.

6. How do you manage DOACs peri-surgery?

Advice will be given to the patient by the preassessment clinic. If this has not occurred or is not clear, then contact the surgical team or local anticoagulation clinic.

Drug	When to stop DOAC therapy pre-operatively		
Dabigatran	Renal function (CrCl ml/min)	High risk of bleeding or major surgery	Standard risk of bleeding
	≥80	48 hours	24 hours
	≥50-<80	48-72 hours	24-48 hours
	≥30-<50	96 hours	48-72 hours
Rivaroxaban	Renal function (CrCl ml/min)	High risk of bleeding or major surgery	Standard risk of bleeding
	≥30	48 hours	24 hours
	<30	72 hours	48 hours
Apixaban	Renal function (CrCl ml/min)	High risk of bleeding or major surgery	Standard risk of bleeding
	≥30	48 hours	24 hours
	<30	72 hours	48 hours
Edoxaban	Renal function (CrCl ml/min)	High risk of bleeding or major surgery	Standard risk of bleeding
	≥30	48 hours	24 hours
	<30	72 hours	48 hours

In the majority of cases, anticoagulation is re-initiated once haemostasis is secure. The DOAC will be restarted by the hospital surgical team or anticoagulation clinic post operatively or LMWH (e.g., dalteparin or enoxaparin) may be used in the interim before the DOAC is restarted as necessary.

If your patient has not had anticoagulation restarted following surgery, please follow up with the surgical team as a plan should be communicated to primary care in all cases.

See: The [Handbook of Perioperative Medicines \(ukcpa-periophandbook.co.uk\)](http://ukcpa-periophandbook.co.uk) for further information concerning type of surgery and bleeding risk and management of anticoagulation perioperatively

7. How should frail patients at high falls risk be managed?

For these patients no dose reduction is required (unless renally impaired or low bodyweight) and anticoagulation should not be withheld if the CHADVASc score is high >2

- A study by Man-Son-Hing et al *Arch Intern Med.* 1999;159:677-685 showed that 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.
- See overprescribing guidance below: Anticoagulation may be stopped in patients with a very high risk of head injury associated with falls after a clearly documented risk: benefit discussion with the patient/family and treating clinicians.
- For all patients with frailty and all patients aged over 75 years: Renal function, liver function and haemoglobin should be monitored every 4 to 6 months ([SPS](#))

8. How do we consider overprescribing when starting or reviewing anticoagulation?

Think Overprescribing..... [Good for you, good for us, good for everybody: a plan to reduce overprescribing to make patient care better and safer, support the NHS, and reduce carbon emissions \(publishing.service.gov.uk\)](#)

1. Is there a better alternative? Consider lifestyle factors. Where continued anticoagulation is appropriate, consider once-daily DOAC such as edoxaban in AF or rivaroxaban in VTE if clinically appropriate to reduce pill burden
2. Is it appropriate for the individual patient? Risk:benefit discussion
3. Is it no longer appropriate due to changes in the patient's circumstances? E.g. EOL, severe renal impairment
4. Does the patient continue to benefit from this medication? Decision aid tool: [ADST \(anticoagulation-dst.co.uk\)](#)
[www.stroke.org.uk](#)
5. Refer patients for specialist support if there are clear contra-indications to anticoagulation or if further advice is required

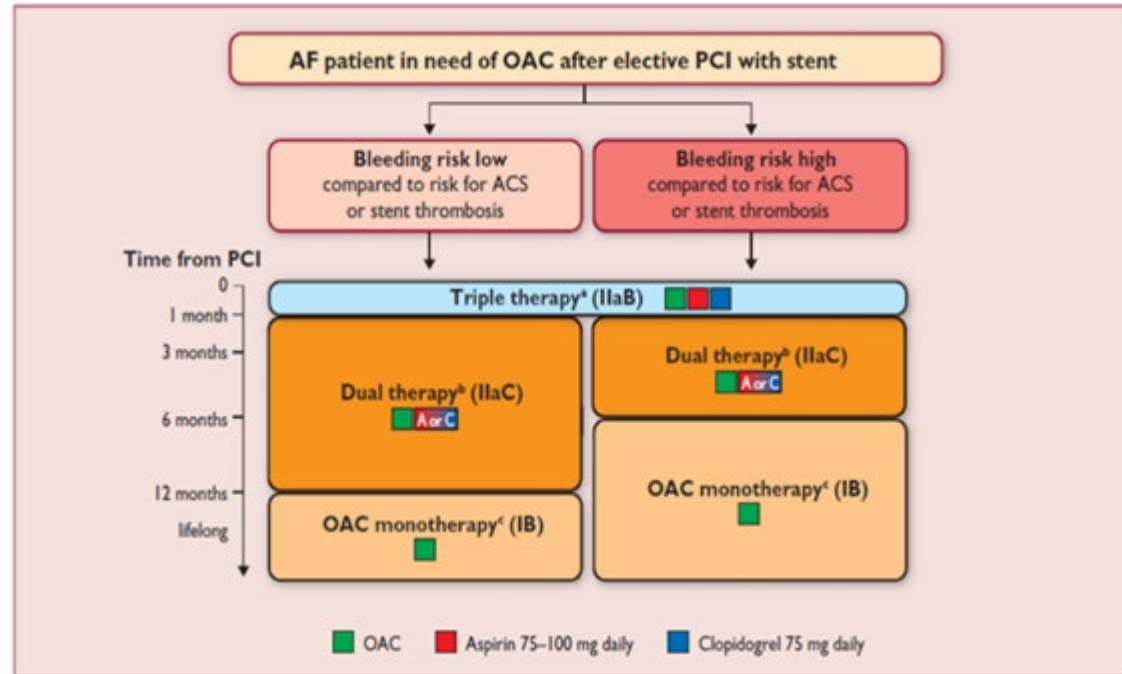
9. When should antiplatelets be reviewed in combination with oral anticoagulation (OAC)?

- 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 other indication than for secondary prevention of cardiovascular events or peripheral vascular disease then it can usually be stopped (*see [UCLP table below](#)*)
- 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 the patient is under the care of a cardiologist, or vascular specialist, seek their advice as balancing the clinical need for anticoagulant and antiplatelets may be a complex decision

Indication for antiplatelets	Antiplatelet	Action when initiating anticoagulation for AF
Primary prevention of CVD	Antiplatelet monotherapy	Stop antiplatelet therapy (antiplatelet therapy not recommended for primary prevention of CVD)
Secondary prevention of CVD <ul style="list-style-type: none"> Stroke / Transient Ischaemic Attack (TIA) Stable coronary heart disease (CHD) Peripheral arterial disease (PAD) 	Antiplatelet monotherapy or Low dose rivaroxaban with aspirin	Stop antiplatelet therapy Increase DOAC dose (to AF stroke prevention dose) and stop aspirin
Patients within 12 months of an ACS or stent placement (cardiac or vascular)	Aspirin plus clopidogrel, ticagrelor or prasugrel	Seek specialist advice to agree the preferred drug regimen. Triple therapy (dual antiplatelet plus anticoagulant) duration must be clearly defined.
Patients more than 12 months after an ACS or stent placement (cardiac or other vascular)	Antiplatelet monotherapy / dual antiplatelet therapy If discharge summary indicates dual antiplatelet required long-term	Stop antiplatelet therapy, unless otherwise advised by specialist (check discharge summary) Seek specialist advice – do not initiate triple therapy without advice
When using an anticoagulant plus an antiplatelet – add a proton pump inhibitor (PPI)		

NB. Please note that for patients prescribed the antiplatelet clopidogrel who require PPI therapy, avoid omeprazole and esomeprazole: [SPS](#), in [SEL](#) lansoprazole or pantoprazole are prescribed South East London Integrated Medicines Optimisation Committee (SEL IMOC). A partnership between NHS organisations in South East London Integrated Care System: NHS South East London (covering the boroughs of Bexley/Bromley/Greenwich/Lambeth/Lewisham and Southwark) and GSTFT/KCH /SLaM/ Oxleas NHS Foundation Trusts and Lewisham & Greenwich NHS Trust

9. When should antiplatelets be reviewed in combination with oral anticoagulation (OAC)?



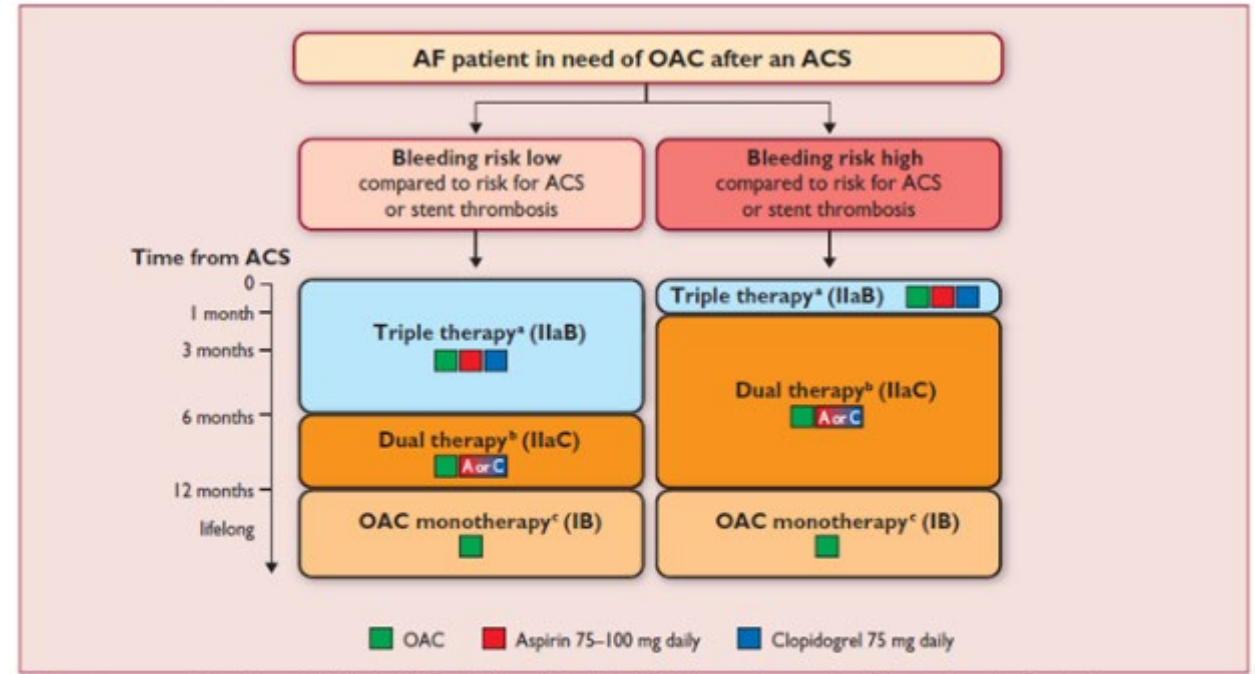
ACS = acute coronary syndrome; AF = atrial fibrillation; OAC = oral anticoagulation (using vitamin K antagonists or non-vitamin K antagonist oral anticoagulants); PCI = percutaneous coronary intervention.

^aDual therapy with OAC and aspirin or clopidogrel may be considered in selected patients.

^bOAC plus single antiplatelet.

^cDual therapy with OAC and an antiplatelet agent (aspirin or clopidogrel) may be considered in patients at high risk of coronary events.

Figure 13 Antithrombotic therapy after elective percutaneous intervention in atrial fibrillation patients requiring anticoagulation.



ACS = acute coronary syndrome; AF = atrial fibrillation; OAC = oral anticoagulation (using vitamin K antagonists or non-vitamin K antagonist oral anticoagulants); PCI = percutaneous coronary intervention.

^aDual therapy with OAC and aspirin or clopidogrel may be considered in selected patients, especially those not receiving a stent or patients at a longer time from the index event.

^bOAC plus single antiplatelet.

^cDual therapy with OAC and an antiplatelet agent (aspirin or clopidogrel) may be considered in patients at high risk of coronary events.

Figure 12 Antithrombotic therapy after an acute coronary syndrome in atrial fibrillation patients requiring anticoagulation.

The tables above are a guide as to how triple therapy should be managed for cardiology indications and the durations you may expect to see, reference: <https://academic.oup.com/eurheartj/article/39/16/1330/4942493>

There is no standardised approach for patients with cerebrovascular or vascular indications for antiplatelets. See NICE CKS, Sept 2023: [Antiplatelet treatment | Health topics A to Z | CKS | NICE](#)

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

- For a new presentation of an apparently unprovoked venous thromboembolism (VTE) to secondary care, patients will be started on low molecular weight heparin (LMWH) if they are undergoing urgent cancer (2 week wait) investigations. If they are diagnosed with cancer DOACs can often be used depending on the type and stage of the cancer and planned treatment. This will be decided by the thrombosis team at the treating hospital.
- 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/VTE should be weighed up in this instance). The oncologist or haematologist investigating the cancer should review 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.

11. Can DOACs be prescribed in patients with malignancy?

AF treatment: Ideally keep on current anticoagulant (DOAC or warfarin) AC specialists will consider drug-drug interactions (with chemotherapy), creatinine clearance (CrCl), site of cancer (e.g. GI/GU and brain mets have a high bleed risk) in DOAC choice and dosing.

Consider bleeding risk and thrombosis risk (cancer not a factor in either HASBLED/ORBIT or CHA2DS2VASc) and patient wishes if de-prescribing anticoagulation.

VTE treatment: Evidence now supports the use of DOACs in active cancer patients. Low-molecular weight heparins (LMWHs) are preferred for patients with gastrointestinal or genitourinary malignancies (with intact lesion) or high risk of bleeding. Consider drug-drug interactions (chemotherapy and novel treatments): [Cancer drug interactions](#)

12. What if my patient has haematuria?

Patients taking DOACs are managed by the normal pathway for the investigation and management of haematuria 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).

The DOAC should be continued whilst awaiting investigations where possible, after assessing the risk of stroke/VTE against the risk of bleeding (involving the patient in this discussion). Where a patient has significant haematuria that is ongoing, or a Hb drop >20g/L where this is the likely source, withholding the DOAC (temporarily while this is investigated) may be appropriate.

Consider the patient's HASBLED score ([HAS-BLED Score for Major Bleeding Risk - MDCalc](#)) or the [ORBIT](#) tool and modifiable risk factors for bleeding, as these should be optimised/minimised when prescribing DOACs.

13. How to manage nosebleed and other minor / nuisance bleeding?

Patients should be counselled on DOAC initiation and at every review that, should nuisance or minor bleeding occur, they can continue the DOAC unless otherwise advised by a healthcare professional. It would be prudent to check FBC, U+E and Renal Profile on presentation.

Nose Bleeds: 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. If first aid measures result in the cessation of bleeding within 10-15 minutes the patient does not need to attend A+E or miss any doses of DOAC.

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. 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. A patient information leaflet on epistaxis can be found here: [Nosebleeds \(Epistaxis\) - UPDATE | ENT UK](#)

Bleeding Gums: 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. Should the bleeding gums be excessive or prolonged, refer the patient to the dentist / periodontist for a thorough dental examination

14. Is there an antidote for DOACs?

Outcomes of major bleeds with DOACs are no worse than those with warfarin even in the absence of clinically available antidotes.

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. Gastrointestinal haemorrhage was more frequent in patients taking DOACs than warfarin.

DOACs have a short half-life so withholding the medication and supportive care should be utilised in all circumstances of major bleeding. Haematology and Emergency departments in hospital have guidance for the use of activated charcoal, tranexamic acid and prothrombin complex concentrates.

Available antidotes ([SEL joint medicines formulary](#)) are **red** category (prescribing and supply by hospital only)

- Idarucizumab ([BNF](#))– for the rapid reversal of dabigatran
- Andexanet alfa for apixaban and rivaroxaban- [NICETA697](#) approved for life threatening GI bleeding only

15. What references are available for dosing queries?

- For DOACs the dose reduction criteria varies between agents and indications. 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/>
- See [slide 4](#) for information on dosing in renal impairment and [SEL IMOC guidance](#)
- Guy's and St Thomas' (GSTT) has a free "Thrombosis Guidelines" app which is available on both android and iphone. This app includes GSTT guidance on treatment and prevention of VTE, DOAC dosing, management of over-anticoagulation and warfarin.

16. How do I find out what medicines interact with DOACs? How do I manage them?

Please refer to the British National Formulary ([BNF](#)) and Summary of Product Characteristics ([SPC](#)) for the DOAC agent for further details

Common interactions to consider are with antiepileptic agents, [HIV antiretrovirals](#), hepatitis antivirals, antifungals, and chemotherapy agents

For oncology drug interactions see: Cancer Drug Interactions from Radboud UMC and University of Liverpool ([cancer-druginteractions.org](#))

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.

17. How do I counsel patients? Who can I refer to?

There is a counselling checklist included as part of the [DOAC initiation and monitoring guidance](#)

There are patient materials available to support patient education, including printed leaflets and websites:

AF Association <https://www.heartrhythmalliance.org/afa/uk/>

British Heart Foundation <https://www.bhf.org.uk/>

For patients with a history of venous thromboembolism: [Thrombosis UK https://thrombosisuk.org/](https://thrombosisuk.org/)

Many of the acute hospital trusts and pharmaceutical companies have their own patient information leaflets (PILs) which should be provided to patients. Guy's and St Thomas' (GSTT) has an information app for patients, providing information videos about AF, amongst other conditions: <https://www.guysandstthomas.nhs.uk/our-services/cardiovascular/medtap.aspx>

Community pharmacists and practice-based pharmacists can also help support DOAC adherence and understanding.

For anticoagulation cards (OAT alert): Supplier for GP Practices now Primary care Support England not Xerox via <http://www.nhsforms.co.uk/> Email: pcse.supplies-leeds@nhs.net OR PCSE.DataManager@nhs.net OR PCSE.AdHoc-MR@nhs.net

18. For housebound patients, how will they be weighed before initiation and for follow ups?

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).

If it is possible for district nursing to help with a patient's weight then consider this option (home weighing scales for example)

19. How do I switch anticoagulation therapy?

- **Check indication and contra-indications for anticoagulation before considering a switch**
- Continued anticoagulant therapy is vitally important in patients with NVAF and VTE.
- According to the summary of product characteristics (SPC: www.medicines.org.uk), discontinue dabigatran or apixaban and start edoxaban or rivaroxaban at the time of the next dose of the oral anticoagulant (e.g. 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 anticoagulation before starting the newly prescribed DOAC in order to negate any wastage (medication costs, dispensing costs/pharmacist time etc).

In all cases exercise clinical judgement and ensure that, if the patient is under a specialist, that they have been consulted (e.g. 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 (contact details on [slide 20](#)).

See SEL guidance: [Guidance for the safe switching of patients on Direct Oral Anticoagulants \(DOAC\) for non-valvular atrial fibrillation \(NVAF\) to edoxaban in South East London](#)

See warfarin to DOAC switching guidance from COVID-19 pandemic, appendix 1: <https://www.england.nhs.uk/coronavirus/wp-content/uploads/sites/52/2020/03/C0077-Specialty-guide-Anticoagulant-services-and-coronavirus-v1-31-March.pdf>

Seek advice and guidance from your local anticoagulation clinic for patients switching from warfarin and for their follow up/monitoring requirements

20. What happens if my patient develops a skin rash on a DOAC?

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.

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. This rare reaction may also be possible with other DOAC agents (as with other medications) but have not been reported in literature.

21. What are the current transfer of care arrangements for DOACs in SEL?

- See SEL IMOC DOAC patient pathways for [NVAf](#) and [VTE](#)
- If initiation of DOAC has occurred in secondary care then:
 - 1 month supply is given for AF indication
 - 3 months' supply for VTE indication(if treatment is to be continued this will be assessed by the AC specialists and longer term management communicated to primary care)
- Initiation and TOC forms are no longer required (formulary status changed to amber 2 in 2020)- information is communicated via clinic letter and discharge letter
- If an anticoagulation switch has occurred, then one month supply is given (unless the patient has a blister pack as supply will be determined by local policies)
- Caution patients with blister packs are most at risk from error during anticoagulation initiation/changes- specialist teams will contact primary care to carry on prescribing for patients with blister packs to reduce the risk of error (over/under anticoagulation)
- Discharge medicines service (DMS) to be considered from specialist services to support communication to community pharmacy

22. Contact details (email) for local anticoagulation services in SEL?

For UHL: LH.Anticoagulation@nhs.net

For QEH: LG.QEAnticoagulant@nhs.net

For PRUH: kch-tr.br-anticoag@nhs.net

For KCH: kch-tr.dh-anticoag@nhs.net

For GSTT: gst-tr.anticoag@nhs.net

Bexley, for community service at Bellegrove surgery: anticoag.bellegrove@nhs.net and The Albion surgery: albion.anticoag@nhs.net

Bromley, for Bromley GP Alliance (BGPA) email: selicb.bgpaanticoagulation@nhs.net