Guidance for the safe switching of patients on anticoagulants for non-valvular atrial fibrillation (NVAF) to the direct oral anticoagulant (DOAC) edoxaban in South East London (SEL)

Developed by SEL Cardiovascular Medicines Working Group
on behalf of the SEL Integrated Medicines Optimisation Committee (IMOC) and
following guidance from the National Institute for Health and Care Excellence (NICE) and NHS England & Improvement (NHSEI)

Implementation and adoption of this guidance is to be decided at practice/PCN/borough level across SEL

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South East London Integrated Medicines Optimisation Committee (SEL IMOC). A partnership between NHS organisations in South East London: South East London Integrated Care System (covering the boroughs of Bexley/Bromley/Greenwich/ Lambeth/Lewisham and Southwark) and GSTFT/KCH /SLaM/ Oxleas NHS Foundation Trusts and Lewisham & Greenwich NHS Trust

Contents

Background for edoxaban as preferred DOAC for NVAF and objectives for SEL

- **Objectives:** NHS savings released from the use of DOACs with the lowest acquisition cost will allow more patients with atrial fibrillation and other cardiovascular disease (CVD) to be diagnosed and treated within primary and secondary care settings in South East London (SEL)

- The aim of this guidance is to support a structured review of patients requiring anticoagulation and to support shared- decision making with the patient concerning DOAC choice:
    - Depending on local priorities and on a case-by-case basis: To safely switch patients with NVAF to a more cost-effective alternative DOAC without compromising patient care and by excluding patients who have a contra-indication to this therapy; always involving patients in the decision-making process (*outlined on pages 5 to 7*)
    - To establish edoxaban as the preferred choice for new patients with NVAF unless there is a specific clinical reason not to do so

- **Background**: Since 2020, SEL guidance has recommended edoxaban first line for stroke prevention in AF and rivaroxaban first line for the treatment and secondary prevention of venous thromboembolism (VTE) where this is clinically appropriate

- From January 2022, a national procurement for DOACs recommended: B1279-national-procurement-for-DOACs-commissioning-recommendations-v1.pdf (england.nhs.uk)
    - For patients commencing treatment for AF: subject to the criteria specified in the relevant NICE technology appraisal guidance, clinicians should use edoxaban where this is clinically appropriate. If edoxaban is contraindicated or not clinically appropriate for the specific patient then, subject to the criteria specified in the relevant NICE technology appraisal guidance, clinicians should then consider rivaroxaban first, then apixaban or dabigatran.
    - For patients already prescribed a DOAC for the treatment of AF: subject to the criteria specified in the relevant NICE technology appraisal guidance, commissioners may wish to consider developing local policy to review patients currently prescribed apixaban, rivaroxaban or dabigatran, where clinically appropriate

- 2021 NICE AF guidance recommends a DOAC first line for anticoagulation: https://www.nice.org.uk/guidance/ng196

- Investment and impact fund for PCNs: https://www.england.nhs.uk/wp-content/uploads/2022/03/B1357-investment-and-impact-fund-2022-23-updated-guidance-march-2022.pdf
    - 2022/23 IIF CVD-05: Percentage of patients on the QOF Atrial Fibrillation register and with a CHA2DS2-VASc score of 2 or more (1 or more for patients that are not female), who were prescribed a direct-acting oral anticoagulant (DOAC), or, where a DOAC was declined or clinically unsuitable, a Vitamin K antagonist- aim for 70-95% on DOAC or clearly document why warfarin is indicated or DOAC declined
    - 2022/23 IIF CVD-06: Number of patients who are currently prescribed edoxaban, as a percentage of patients on the QOF Atrial Fibrillation register and with a CHA2DS2-VASc score of 2 or more (1 or more for patients that are not female) and who are currently prescribed a direct-acting oral anticoagulant (DOAC): aim for 25-35% edoxaban prescribing of total DOAC prescribing

- Structured medication review (SMR) focus to reduce the risk of harm to patients from medication errors: Report template - NHSI website (england.nhs.uk)
    - 2022/23 SMR-02C: Aim for 75-90% of patients aged 18 years or over prescribed both an oral anticoagulant and an anti-platelet in the last three months of the previous financial year, who in the three months to the reporting period end date were either (i) no longer prescribed an anti-platelet or (ii) prescribed a gastroprotective in addition to both an oral anticoagulant and an anti-platelet.
    - 2022/23 SMR-03: aim for 50-75% of patients prescribed a direct oral anti-coagulant, who received a renal function test and a recording of their weight and Creatinine Clearance Rate, along with a recording that their DOAC dose was either changed or confirmed not changed.

Identifying Patients Suitable For A Switch to Edoxaban

- Practice-based EMIS search of patients on the AF register:
  - Adults >18 years prescribed apixaban, dabigatran, rivaroxaban or warfarin with NVAF but no valid exclusion criteria (*see page 5*)
  - Populate an excel spreadsheet with required information from medical records (*example given on page 14*)
  - Ensure patients who require additional reviews are referred to a specialist or follow up is scheduled in primary care
  - Consider **prioritising** patients suitable for a switch if non adherent to current regime, not tolerating current regime, or requiring a dose change

- Ensure each patient has had recommended monitoring for anticoagulation within the last 3 months:
  - Patients without documented results will require a full renal profile including a creatinine clearance (CrCl) calculation, up to date body weight (within the last year), FBC and LFTs before considering a switch. It is also good practice to check BP, pulse and lipid profile in CVD patients
  - Ensure monitoring continues to be scheduled with regular follow ups as recommended in SEL DOAC initiation/monitoring guidance

- Consider prioritising patients who may require a structured medication review (SMR):
  - to review concomitant medications and the need for gastro-protection e.g. antiplatelets, antidepressants (SSRIs, SNRIs), anti-inflammatories (NSAIDs) and corticosteroids with anticoagulation (specialist advice may be required)

- Schedule face to face or telephone appointments: *(See page 13 for a template letter inviting patients for an anticoagulation review)*
  - Individual HCPs should work within their area of competence or seek specialist support (a review of the patient list with a specialist is recommended- local policies may differ)
  - Document actions taken in medical notes and schedule follow ups for DOAC monitoring and adherence checks as recommended in SEL DOAC initiation/monitoring guidance

- Involve community pharmacy:
  - If a switch is possible, ensure the patient's community pharmacist is aware of the switch and is able to support the patient with medication supplies and adherence to the anticoagulation regime (a telephone discussion is recommended and a patient referral/add to prescription for the new medicines service-NMS)

Exclusion Criteria for Edoxaban Switching and Contra-indications

Do NOT switch to edoxaban if…	Contra-indications to all DOACs:
A specialist has clearly stated a clinical reason for DOAC choice or warfarin at initiation of anticoagulation: *discuss with the specialist patients prescribed warfarin or any patient concerns with current therapy/regime*	**Valvular AF** ie. AF with moderate to severe mitral stenosis
Patient has an **intolerance** or hypersensitivity to edoxaban: *keep on current anticoagulant if well tolerated*	Severe renal impairment **CrCl <15ml/min** or dialysis patients (*unless under AC specialist*)
MI/ACS/PCI within the last year; patient requires triple therapy (anticoagulation plus dual antiplatelets)- *review the antiplatelet/anticoagulation and dosing when the antiplatelet review is required (as per cardiology/haematology advice) and annually*	**Mechanical heart valves** (metallic) or within 3 months of a bioprosthetic (tissue) valve
Recent VTE within the last 6 months: *ensure patient has been reviewed by AC team and a plan has been communicated concerning course length for anticoagulation*	**Pregnant, breastfeeding** or planning a pregnancy
DOAC therapy associated with **unlicensed indications** eg LV thrombus, arterial thrombus, portal vein thrombosis, antiphospholipid syndrome (APLS)- *these patients are managed by an anticoagulation specialist*	**Concomitant use of medicines** contraindicated with DOACs (see individual DOAC SPCs)
Patient has a history of **menorrhagia** (heavy menstrual bleeding): *for pre-menopausal women check FBC and iron and refer to gynaecology as indicated*	
Patient takes warfarin and requires an **INR higher** than standard 2-3 range: *keep on warfarin*	
Patient is **obese-** weight >120kg: rivaroxaban or apixaban are preferred DOACs in obesity *If Patient is >150kg: do not switch- refer to AC clinic if patient has concerns about current regime*	
Patient has **low bodyweight** <50kg: *therapeutic drug monitoring may be required*	
High creatinine clearance CrCl >95ml/min: *Decreased efficacy for edoxaban observed in a clinical study in patients with a very good renal function compared to warfarin so consider individual thromboembolic and bleeding risks and alternative DOAC options*	
Capacity issues: patient may not be able to understand/agree to switching or cannot follow drug regime	

Special Patient-Specific Circumstances to Consider and Recommended actions….

Special Circumstances	Recommended action
Bleeding risk/active bleeding: *(excludes single episode fully investigated haematuria or isolated episode minor provoked nosebleed)* • Patients with clinically relevant non-major bleeding or a recent major bleed (within last 3 months) • Patients with AAA and major haematoma • Active clinically significant bleeding • Major bleeding risk: recent GU ulceration; neoplasms; recent brain or spinal injury; recent brain, spinal or ophthalmic surgery; recent intracranial haemorrhage; oesophageal varices; arteriovenous malformations; vascular aneurysms; major intraspinal or intracerebral vascular abnormalities (see SPC)	**Do not switch/initiate edoxaban**: Clinical review required and refer to specialist to consider whether anticoagulation is appropriate
Hepatic disease associated with coagulopathy and clinically relevant bleeding risk	For raised LFTs: AST/ALT (>2xULN), Bilirubin (>1.5xULN) refer to anticoagulation (AC) specialist and liver specialist. Check SPC for DOAC prescribing guidance/contra-indications according to Child Pugh score
Any **cancer/active malignancy/chemotherapy**	Seek specialist advice (advice and guidance- A&G) from the AC team concerning anticoagulation options
Haemoglobin (Hb) <100g/L or consider higher value if elderly/frail/low weight	Investigate cause, manage e.g. iron deficiency, and refer to appropriate specialist (including 2 week wait pathway) as indicated: anticoagulation may require a temporary cease
Platelets <100 $x10^9$/L	Monitor closely and investigate further- advise patient to report any bleeding. Refer platelets <50 to clinical haematology and stop anticoagulation until specialist review
Uncontrolled severe hypertension: SBP >170mmHg and/or DBP >100mmHg	Clinical review required to manage hypertension (NICE guidance), reduce blood pressure and reduce bleeding risk and cardiovascular risk reduction in patients taking anticoagulation
Prescribed interacting medicines: • check antivirals, antiretrovirals, rifampicin and antiepileptics* that may reduce DOAC levels (BNF, SPC) • reduce edoxaban dose with P-gp inhibitors that may increase DOAC levels: ciclosporin, dronedarone, erythromycin, ketoconazole ***AED:** phenytoin, carbamazepine, phenobarbitone	Refer to SPC, adjust dose as indicated and consider advice from AC specialist. For patients prescribed potent CYP3A4 or P-gp inducers or inhibitors- seek A&G or refer to AC specialist for anti-Xa monitoring and anticoagulant choice/dosing guidance HIV drug interactions https://www.hiv-druginteractions.org/
Short term use: Scheduled for planned cardioversion with CHA2DS2-VASc score 0	Edoxaban is the preferred agent for this but ensure DOAC is reviewed 4 weeks post cardioversion by electrophysiology/cardiology. DOAC may be prescribed longer term if advised by cardiology and/or the CHA2DS2-VASc score >1
If unconfirmed AF or CHA2DS2Vasc score <1	Review if any other indication for anticoagulation and consider stopping DOAC therapy. If patient is due for 24h tape or 7-day Holter monitor do not stop anticoagulation until AF has been ruled out by ECG
High falls risk/frail patients: Generally anticoagulation should not be withheld or the dose unnecessarily reduced if high CHA2DS2Vasc score and/or frailty, but you/your patient may have concerns about a cerebral bleed risk and a risk:benefit discussion will be required and documented	Refer to local falls clinic or haematologist if you have risk:benefit concerns for anticoagulation. Monitor renal function, liver function and haemoglobin every 6 months for frail patients regardless of age
Adherence issues: Identify the underlying cause for this and manage modifiable risk factors for non-adherence	Exercise clinical judgement and do not switch or consider a therapy review. Involve multi-disciplinary team (MDT), family/carers and community pharmacy to support follow up
Swallowing difficulties	Edoxaban may be crushed and mixed with water or apple puree and immediately administered orally. For enteral tubes: the location of the feeding tube and site of absorption of the medication needs to be considered. There is a limited evidence base for LMWH as an alternative anticoagulation in patients with AF

Shared decision-making process

- Explain the circumstances and reasoning for medication change with the patient: (*see DOAC comparison table on page 11 and template patient letter on page 13*)

Discuss	Recommended actions
Bleeding risk and history	Explore any interventions that may help to reduce this (ORBIT and HASBLED tools)
Stroke risk	CHA2DS2-VASc: compare anticoagulation to taking no action and discuss DOAC choice (*see page 11*)
Renal function	Calculate creatinine clearance (CrCl) with actual body weight from within last 12 months and serum Cr from within 3 months (for patients >120kg use adjusted bodyweight- see SEL renal monitoring guidance for DOACs
Age	For edoxaban there are no adjustments to dosing based on age (NB. all DOACs are not recommended <18years for AF indication)
Bodyweight	Check bodyweight in all patients to determine renal function. Reduce edoxaban dose to 30mg in patients <60kg- seek advice from AC team for initiation in obese patients >120kg (*see exclusion criteria page 5*) and low weight <50kg
Co-morbidities	See exclusion criteria *page 5* and special circumstances *page 6*
Management of bleeding	Most bleeding is managed through temporarily stopping the DOAC and supportive care. Prothrombin complex concentrate (PCC) is commonly used in severe bleeding but no reversal agent is currently available for edoxaban. If the patient requires further information on reversal agents see *page 12.*
Dosing regime/DOAC choice	Consider once daily v twice daily and lifestyle/routine. Also consider with and without food options and established medication regime frequency burdens (*see page 11 for DOAC agent comparison table*)
Drug interactions	Check SPC and BNF but also consider effect of herbal remedies such as St John's wort, and over the counter medicines/vitamins
Food interactions	Edoxaban is not taken with food but doses of rivaroxaban ≥15mg must be taken with food to aid absorption
Prior warfarin/DOAC experience	Explore tolerability with the patient
DOAC counselling and adherence support	*See page 12* for a DOAC counselling checklist. Encourage regular medication adherence with regular scheduled follow up appointments and referrals to community pharmacy
Document	In medical notes record any discussions/questions and the decision-making process

How to switch from warfarin to edoxaban?*

*Ensure there are no contra-indications to DOAC therapy, specific patient circumstances or exclusion criteria for edoxaban (*pages 5 to 6*)- **do not switch if any apply to your patient**

*Follow a decision- making process (*example on page 7*) including all options with your patient and document consent for the switch/initiation- **if consent is not possible keep on current regime**
It is advised to re-check CHA2DS2-VASc and HASBLED/ORBIT to determine risk:benefit of anticoagulation and to address modifiable risk factors for bleeding before changing therapy.

Check recent U&Es, LFTs and FBC (from within last 3 months) and calculate creatinine clearance (CrCl) using actual bodyweight (from within the last 12 months) *use adjusted bodyweight in patients >120kg*

Check INR

*EHRA guidance on when to start DOACs after stopping warfarin:
If INR < 2: commence DOAC that day
If INR 2 to 2.5: commence DOAC on the next day ideally (or the same day)
If INR 2.5 to 3: withhold warfarin for 24 to 72 hours and then initiate DOAC
Reference: https://academic.oup.com/eurheartj/article/39/16/1330/4942493?guestAccessKey=e7e62356-8aa6-472a-aeb1-eb5b58315d49

Advise patient when to stop warfarin in relation to starting edoxaban:
INR should be <2.5 before starting edoxaban (see EHRA guidance)

Prescribe edoxaban at an appropriate dose according to renal function, bodyweight and any interacting medications

Dosing in renal impairment*: If your patient is a dialysis patient do not switch from warfarin without consulting a specialist*

for <15ml/min: All DOACs contra-indicated (Dabigatran is contra-indicated <30ml/min)

15 to 49ml/min: edoxaban 30mg once daily

50 to 95ml/min: edoxaban 60mg once daily

CrCL >95ml/min: A trend towards decreasing efficacy with increasing CrCl was observed for edoxaban compared to well-managed warfarin. MHRA alert: Edoxaban should be used in patients with NVAF and high CrCl (>80ml/min) only after a careful evaluation of the individual thromboembolic and bleeding risk. In SEL edoxaban is cautioned at CrCL >95ml/min as per SPC- prescribe alternative DOAC

Commence edoxaban 60mg once daily.
Reduce dose to 30mg once daily if:
Body weight <61kg
or CrCl <50ml/min
or co-prescribed with ciclosporin, dronedarone, erythromycin or ketoconazole

Prescribe edoxaban at appropriate dose (SPC) and advise patient to obtain supplies from their chosen pharmacy.
Ensure that the active medication list is updated and that edoxaban is the only anticoagulation on the repeat list of medications.

Remove warfarin from the repeat prescription after initiating edoxaban and inform the community nursing teams (*if applicable*) monitoring warfarin dosing and INR for your patient that warfarin has stopped. *It is advised to work collaboratively with the anticoagulation team throughout the switch.

Provide written instructions and involve family members/carers where possible to minimise the risk of patients taking warfarin and DOAC concurrently.
Encourage the return of current warfarin supplies and blister packs to the patient's pharmacy to reduce the risk of error.

*It is recommended that these patients are switched in collaboration with the anticoagulation specialist/clinic: local pathways may differ- either clinic referral or A&G or virtua review- *see AC contact details on page 15*

Inform the patient's community pharmacy of the change in anticoagulation especially for patients with medication compliance aids and encourage a new medicines service (NMS) review with the pharmacist

If the switch to DOAC has occurred outside the GP practice, provide accurate information relating to indication, baseline tests and monitoring requirements to allow primary care to safely take over prescribing responsibility following DOAC initiation. For the patient/carer, provide an up to date anticoagulation card and DOAC counselling (*see page 12*)

Schedule follow up appointments in primary care, using the clinical system recall function: **after 1-3 months:** check for bleeding issues, side effects, tolerability and adherence support; **at least annually check:** renal profile, FBC and LFTs- frequency depends on renal function, age and frailty (*see SEL renal monitoring guidance*)- 6 monthly checks are required for aged >75 years and frail patients

How to switch from dabigatran or apixaban to edoxaban?

Review with the patient any special circumstances/exclusion criteria where an edoxaban switch may not be the recommended action (*see pages 5 & 6*)- **if any apply keep on dabigatran/apixaban**

If for NVAF: check if the patient is suitable for and able to consent to an edoxaban switch and check if an antiplatelet review is required (*schedule an SMR*)

Follow a decision- making process (*example on page* 7) including all options with your patient (*page 11*) and document consent for the switch/initiation- **if consent is not possible keep on current regime**

Check clinical system for recent U&Es, LFTs and FBC (within last 3 months)

Calculate creatinine clearance (CrCl) with actual body weight from within last 12 months (unless recent weight loss/gain) and serum creatinine check from within last 3 months

Dosing in renal impairment: for <15ml/min: All DOACs contra-indicated (Dabigatran is contra-indicated <30ml/min). *If your patient is a dialysis patient please consult a specialist/refer to AC clinic*

15 to 49ml/min: edoxaban 30mg once daily

50 to 95ml/min: edoxaban 60mg once daily

CrCL >95ml/min: A trend towards decreasing efficacy with increasing CrCl was observed for edoxaban compared to well-managed warfarin. The MHRA alert states: Edoxaban should be used in patients with NVAF and high CrCl (>80ml/min) only after a careful evaluation of the individual thromboembolic and bleeding risk. In SEL edoxaban is cautioned at CrCL >95ml/min as per SPC- **do not switch these patients unless advised to by a local AC specialist**

Prescribe edoxaban at appropriate dose (SPC) and advise the patient to obtain supplies from their chosen pharmacy before scheduling a day for the switch.
Ensure that the active medication list is updated on the primary care record and that **edoxaban is the only anticoagulation on the repeat list of medications**.

Advise the patient when to stop apixaban or dabigatran in relation to starting edoxaban: ideally switch to edoxaban the day after using up their existing supply of dabigatran/apixaban (*or ask patient to return current supplies to their community pharmacy*)- take both morning and evening doses of apixaban/dabigatran on the day before the switch **and then take edoxaban once a day on the following day**

Provide written instructions and involve family members / carers where possible to minimise the risk of patients taking both apixaban/dabigatran and edoxaban concurrently, or to avoid twice daily administration of edoxaban. Particular care should be taken where patients are using medication compliance aids to minimise the risk of incorrect dosing.
Ensure the patient understands that the edoxaban should only be taken ONCE daily.

Provide an up-to-date Anticoagulant Alert card and DOAC counselling (*see page 12*) for the patient/carer

If the DOAC switch is undertaken outside of the GP practice, provide accurate information relating to indication, baseline tests and monitoring requirements to primary care to enable safe prescribing

Inform community pharmacy of the change and encourage follow up via NMS/DMS for adherence support

Schedule follow up appointments in primary care (use the clinical system recall function):
after 1-3 months: check for bleeding issues, side effects, tolerability and adherence support
at least annually check: renal profile, bodyweight, FBC and LFTs- frequency depends on renal function, age and frailty (see *SEL renal monitoring guidance*)- 6 monthly checks are required for aged >75 years and frail patients.
It is also good practice to check BP, pulse and lipid profile at least annually to manage CV risk.

How to switch from rivaroxaban to edoxaban?

Check the indication for anticoagulation and if there are patient specific circumstances for rivaroxaban therapy?

If for VTE, on 2.5mg bd dose for CAD/PAD, under a specialist management, or if any exclusion criteria/ patient specific circumstances apply (*pages 5 to 6*)- **do not switch to edoxaban and continue rivaroxaban therapy**

If for NVAF: check if patient consents to edoxaban switch and check if an antiplatelet review is required (*schedule an SMR*)

Check U&Es, LFTs and FBC from within last 3 months: investigate any results outside of normal ranges

Calculate creatinine clearance (CrCl) with actual bodyweight (from within last 12months) or use ideal bodyweight if weight >120kg and with serum creatinine (from within last 3 months)

If CrCl <15ml/min: DOAC contra-indicated-refer to specialist. *If your patient is a dialysis patient please consult a specialist/refer to AC clinic*

If CrCl **15-49ml/min:** edoxaban 30mg once daily

If CrCl **50-95ml/min:** edoxaban 60mg once daily

If CrCl >95ml/min: continue rivaroxaban therapy as edoxaban is cautioned

Edoxaban dosing: Commence edoxaban 60mg once daily.
Reduce dose to 30mg once daily if:
Body weight <61kg
or CrCl <50ml/min
or co-prescribed with ciclosporin, dronedarone, erythromycin or ketoconazole

After shared decision-making with the patient (*see page 7*), prescribe edoxaban at the appropriate dose considering renal function, body weight and drug interactions (SPC)

Make a plan for the switch depending on supplies of current DOAC medication or ask patient/carer to return current anticoagulation medication to the pharmacy- stop rivaroxaban on one day and **start edoxaban once daily on the following day**

Ensure written information is given to the patient/carer, the anticoagulation card is updated, community pharmacist and primary care are informed of the change to DOAC and patient is referred for adherence/counselling support at their chosen community pharmacy (*see counselling checklist on page 12*)

Schedule follow up appointments in primary care (use the clinical system recall function):

after 1-3 months: check for bleeding issues, side effects, tolerability and adherence support

at least annually check: renal profile, bodyweight, FBC and LFTs- frequency depends on renal function, age and frailty (see *SEL renal monitoring guidance*)- 6 monthly checks are required for aged >75 years and frail patients. It is also good practice to check BP, pulse and lipid profile at least annually to manage CV risk.

DOAC comparison table

- It is for the prescribing clinician to determine which DOAC(s) are clinically appropriate for an individual patient based upon the relevant NICE TA guidance:

DOAC	Edoxaban	Rivaroxaban	Apixaban	Dabigatran
Dosing in Non-valvular AF (lifelong unless risk:benefit of anticoagulation therapy changes)	Prescribe Edoxaban 60mg once daily Reduce dose to 30mg once daily if: Body weight <61kg, or CrCl< 50ml/min, or co-prescribed with ciclosporin, dronedarone, erythromycin or ketoconazole.	Prescribe Rivaroxaban 20mg once daily Reduce dose to 15mg once daily if CrCl< 50mL/min in NVAF patients only.	Prescribe Apixaban 5mg twice daily Reduce dose to 2.5mg twice daily if at least two of the following characteristics: age ≥ 80 years, body weight ≤ 60 kg, or serum creatinine ≥ 133 micromol/l or if exclusive criteria of CrCl 15 - 29 ml/min.	Prescribe Dabigatran 150mg twice daily if aged <75 years, CrCl> 50mL/min, low risk of bleeding (weight <50kg with close clinical surveillance) Reduce dose to 110mg twice daily if aged > 80 years or prescribed verapamil. Consider 110mg twice daily based on individual assessment of thrombotic risk and the risk of bleeding in patients aged between 75 and 80 years or with CrCl <50mL/min or with increased risk of bleeding (including gastritis, oesophagitis, gastro-oesophageal reflux).
Contraindicated / Not recommended	CrCl <15ml/min	CrCl <15ml/min	CrCl <15ml/min	CrCl <30ml/min
Cautions **See also individual SPCSs**	CrCl >95ml/min	CrCl <30ml/min. Take with or after food (15mg and 20mg doses)		Do not use in a standard medication compliance aids (MCA)
Interactions **Check BNF:** **www.bnf.org** **SPC:** **www.medicines.org.uk**	Rifampicin, phenytoin, carbamazepine, phenobarbital or St. John's Wort – use with caution Ciclosporin, dronedarone, erythromycin, ketoconazole – reduce dose as above. (See BNF and SPC for edoxaban for further information)	Ketoconazole, itraconazole, voriconazole, posaconazole, ritonavir, dronedarone – not recommended (See SPC for full details) Rifampicin, phenytoin, carbamazepine, phenobarbital, St. John's Wort – Should be avoided.	Ketoconazole, itraconazole, voriconazole, posaconazole, ritonavir - not recommended (See SPC for full details) Rifampicin, phenytoin, carbamazepine, phenobarbital, St. John's Wort – use with caution. Do not use apixaban with patients on strong enzyme inducers for acute VTE treatment	Ketoconazole, ciclosporin, itraconazole, tacrolimus, dronedarone - contraindicated (See SPC for full details) Rifampicin, St John's Wort, carbamazepine, phenytoin –should be avoided. Amiodarone, quinidine, ticagrelor, posaconazole – use with caution. Verapamil (use reduced dose). Antidepressants: SSRIs and SNRIs- increased bleeding risk

Counselling checklist for DOACs

Counselling points	Sign/tick
Explanation of an anticoagulant (increases clotting time and reduces risk of clot formation) **and explanation of indication for therapy** (atrial fibrillation and stroke risk reduction)	
Differences between DOAC and warfarin (if applicable 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/safe limits) • **Fewer drug interactions**	
Name of drug: generic & brand name	
Explanation of dose: strength & frequency	
Duration of therapy: indefinitely/lifelong for AF (unless risk:benefit of anticoagulation changes/patient circumstances change)	
To take with food (dabigatran and rivaroxaban). Not required for apixaban or edoxaban	
If missed doses: Message is to "take the dose as soon as you remember and then at the same time each day". For further information: • **Edoxaban and rivaroxaban** can be taken within 12 hours of missed dose, otherwise omit the missed dose • **Apixaban and dabigatran** can be taken within 6 hours of missed dose, otherwise omit the missed dose	
If extra doses taken: obtain advice immediately from pharmacist/GP/NHS Direct (111)	
Importance of adherence: short half-life and associated risk of stroke and/or thrombosis if non-compliant	

Counselling points	Sign/tick
Common and serious side-effects and who/when to refer: symptoms of bleeding/unexplained bruising. Avoidance of contact sports. • Single/self-terminating bleeding episode – routine appointment with GP/pharmacist • Prolonged/recurrent/severe bleeding/head injury – A&E Major bleeds are managed with temporary interruption of medication and supportive measures including Prothrombin Complex Concentrate (PCC). Specific reversal agents are also available, but rarely required: *Idarucizumab for dabigatran (NICE TA); andexanet alfa for apixaban, rivaroxaban (NICE TA). Access to andexanet alfa is in line with NICE TA criteria for its use.*	
Drug interactions and concomitant medication: avoid NSAID's. Always check with a pharmacist regarding OTC/herbal/complimentary medicines	
Inform all healthcare professionals of DOAC therapy: GP, nurse, dentist, pharmacist i.e. prior to surgery	
Pregnancy and breastfeeding: potential risk to foetus – obtain medical advice as soon as possible if pregnant/considering pregnancy. Avoid in breastfeeding	
Storage: dabigatran must be kept in original packaging – moisture sensitive. All other DOAC are suitable for standard medication compliance aids/ dosette boxes if required	
Follow-up appointments, blood tests, and repeat prescriptions: ensure the patient has details of where, when and how often?	
Issue relevant patient information AF booklet/leaflet and anticoagulant patient alert card	
Give the patient the opportunity to ask questions and encourage follow up with community pharmacist (NMS – New Medicines Service)	

Appendix 1: template letter example inviting patients for an anticoagulation review

(a word document version is available on the SEL IMOC website)

GP practice details:
Contact telephone:
Date:

Dear ,

We are conducting a review of patients prescribed anticoagulation (also known as "blood thinning medication") to reduce the risk of a stroke in patients with atrial fibrillation ("a condition that causes an irregular and often abnormally fast heart rate") in our practice.

The aim is to:

- support patients with their anticoagulation therapy
- ensure appropriate monitoring and dosing of medicines
- determine the best choice of medication for each patient.

We are writing to you as: (*delete lines or tick boxes as appropriate*)

- ☐ We would like to arrange for you to have a review of your medicines with our practice-based pharmacist concerning your medications- please contact the practice receptionist to make an appointment
- ☐ We would like to offer you a blood test to check your kidney function, full blood count and/or liver function- please book an appointment with the nurse or healthcare assistant at your earliest convenience
- ☐ We would like to check your blood pressure- if you are checking this at home then please let us know the reading or contact the practice receptionist to have it checked
- ☐ We would like to invite you for a face- to -face appointment with your doctor
- ☐ We would like to refer you to the anticoagulation clinic for a review
- ☐ We would like to know a recent and up to date bodyweight, if you have weighing scales at home, please submit readings to your surgery, via (text message/ email/ letter/ telephone call) (*delete as appropriate*) or please drop into the surgery to use the weighing scales in the patient waiting area and give the results to our reception staff

We are here to help you and look forward to hearing from you. **Please do not hesitate to contact us if you would like further information or have any questions on this:**

The practice-based pharmacist (*insert name*) on (*telephone number and/or email address*)

Resources for patients:

- on atrial fibrillation: Atrial Fibrillation - Arrhythmia Alliance - UK (heartrhythmalliance.org)
- for anticoagulation, see the NHS website: https://www.nhs.uk/conditions/anticoagulants/ and British Heart Foundation: https://www.bhf.org.uk/informationsupport/heart-matters-magazine/medical/drug-cabinet/novel-anticoagulants

Yours sincerely,

Appendix 2:
Example of data collection for practice-based DOAC patient reviews in primary care (an excel template is available on the SEL IMOC website)

EMIS number	Age (years)	Gender	Bodyweight (kg)	Date	Serum Cr (µmol/L)	Date	CrCl (ml/min)	Date	LFTs	Date	Hb	Date	Platelets	Date	DOAC	Dose	Under specialist?	Interactions?	Indication
e.g. 289676	76	f	70	4.4.22	120	4.4.22	39	4.4.22	normal	4.4.22	150	4.4.22	300	4.4.22	apixaban	2.5mg bd	no	no	AF

Dose change?	Switch?	DOAC CI?	Action required: eg. check bloods, refer, switch, book appt	Follow up scheduled?
yes if stay on apixaban increase dose to 5mg bd as CrCl >30, age <80, wt >60, Cr <133	yes to edoxaban 30mg as CrCl <50ml/min	no	Patient consent for switch and follow up 3-6 monthly according to CrCl and age	F2F appointment

Contact details for local anticoagulation services in SEL

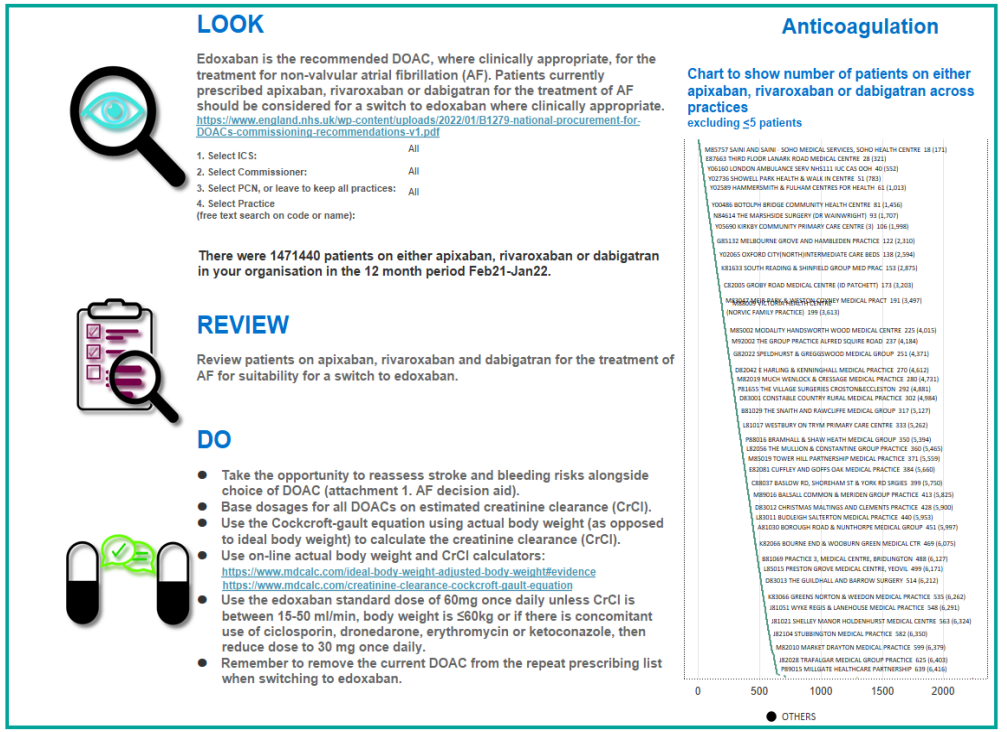
It is recommended that primary care use advice and guidance via eRS for further support from local anticoagulation clinics. Generic anticoagulation clinic email contacts may be used for non-urgent queries about warfarin management for patients managed at that clinic:

For all anticoagulation queries, including switching advice:

use eRS for advice and guidance

Anticoagulation Service	Email contact
University Hospital, Lewisham	LH.Anticoagulation@nhs.net
Queen Elizabeth Hospital, Greenwich	LG.QEAnticoagulant@nhs.net
Princess Royal University Hospital	kch-tr.br-anticoag@nhs.net
King's College Hospital	kch-tr.dh-anticoag@nhs.net
Guys and St Thomas' NHS Foundation Trust	gst-tr.anticoag@nhs.net
Bexley, for community clinic service	anticoag.bellegrove@nhs.net
Bromley, for Boots community pharmacy service	muhammad.patel@boots.co.uk

There are supporting documents on PrescQIPP that may help with patient consultations such as an Edoxaban PIL and learning tools: https://www.prescqipp.info/our-resources/bulletins/bulletin-282-anticoagulation/



Glossary of terms

- AAA: abdominal aortic aneurysm
- HCP: healthcare practitioner
- MI: myocardial infarction
- ACS: acute coronary syndrome
- PCI: percutaneous coronary intervention
- VTE: venous thromboembolism
- LV: left ventricle
- INR: international normalised ratio
- SBP: systolic blood pressure
- DBP: diastolic blood pressure
- CYP3A4: cytochrome P450 3A4 enzyme
- P-gp: P-glycoprotein
- AST: aspartate aminotransferase
- ALT: alanine transaminase
- EHRA: European Heart Rhythm Association
- SMR: structured medication review

Supporting guidance/references

- SEL IMOC DOAC guidance:
  - DOAC FAQs for primary care
  - DOAC initiation and monitoring template/guidance
  - DOAC patient pathway for NVAF
  - Calculating renal function for DOAC patients
  - Initiation of anticoagulation for NVAF
- National guidance on prescribing anticoagulation in NVAF
- SPC for edoxaban
- BNF for edoxaban