South East London Integrated Medicines Optimisation Committee (SEL IMOC)

Direct Oral Anticoagulant (DOAC) Initiation and Monitoring Guidance for Non- Valvular Atrial Fibrillation (AF)

Please note that the initiation and monitoring recommendations in this document apply to patients with the atrial fibrillation (AF) indication and NOT for patients with deep vein thrombosis (DVT) or pulmonary embolism (PE) or other venous thromboembolism (VTE). The dosing recommendations and DOAC choice are different for VTE patients and this guidance should not be referred to for these patients.

Approval date: February 2024, minor updates approved August 2024
Review date: February 2026 (or sooner if evidence or practice changes)

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

Direct Oral Anticoagulant (DOAC) Initiation and Monitoring Guidance for Non- Valvular Atrial Fibrillation (AF)

1 ***Which Patients?*** Assess need **and offer/refer for anticoagulation (using local referral form on DXS):**

- Non-Valvular AF/Atrial Flutter
- CHA2DS2-VASc ≥2 (consider ≥1 for men)
- A cardioversion/ablation procedure when advised by a cardiology specialist (*started regardless of CHA2DS2-VASc score. If the score is 0, then patients do not require long term anticoagulation following the procedure*)

2 ***Does the patient have a contraindication to DOAC? If YES to any of the below – refer to anticoagulation specialist***

- Known intolerance to anticoagulation/previous serious bleed (consider a lesion or condition that is a significant risk for major bleeding e.g. current or recent gastrointestinal ulceration, known or suspected oesophageal varices)
- Hepatic disease associated with coagulopathy
- Mechanical heart valve
- Transcatheter aortic valve implantation within last 3/12
- Mitral valve replacement or repair within last 3/12
- Known moderate to severe mitral stenosis (valvular AF)
- Active or underlying cancer
- Pregnant/breastfeeding or planning a pregnancy
- Triple positive antiphospholipid syndrome (APLS)

3 **Assess for initiation of DOAC**

Parameter	Action	When to refer
Actual weight	- Measured within the last year	- < 50kg or >150kg
Creatinine clearance (CrCL)	- Refer to calculating renal function guidance (do NOT use eGFR or ideal body weight for CrCL) - Review nephrotoxic medication if CrCL is reduced. Please see Guidelines for Medicines Optimisation in patients with Acute kidney Injury	- CrCL < 30ml/min (if CrCL < 15ml/min, DOAC is contra-indicated- requires a warfarin referral/consideration) - Dialysis patients - CrCL > 95ml/min (**The use of edoxaban is cautioned** – use alternative DOAC)
Blood results (within the last month)	- U&Es - serum creatinine (Cr) - FBC – Haemoglobin (Hb), platelets (Plts) - LFTs – AST/ALT, bilirubin and baseline clotting screen	- Hb low (<100g/l) with no identifiable cause, plts <100 units. - LFTs - >2 X ULN, bilirubin > 1.5 x ULN, abnormal clotting screen.
Bleeding risk HASBLED or ORBIT score	- Modify risk factors to reduce bleeding e.g., BP control, use of NSAIDs, alcohol, obesity - HASBLED - ORBIT	- Gastrointestinal/genitourinary bleed within 3/12 - intracranial haemorrhage within 6/12 - severe menorrhagia - known bleeding disorders - known cirrhosis
Alcohol	- Aim < 8 units per week	- Known liver cirrhosis
Blood pressure (BP) mmHg	- Address uncontrolled hypertension- systolic BP > 140mmHg	- If SBP >180mmHg same day review
Concurrent medication	- Antiplatelets- review course length and indication - NSAIDs- bleeding risk - Drug interactions – Refer to SPC, BNF and HIV drug interaction checker - Swallowing difficulties – refer to NEWT	- Dual antiplatelet therapy- cardiologist should specify time period for prescription post CVD event/intervention - Antiplatelet – co-prescribing should be avoided unless advised by specialist - Contraindications and interactions (ask pharmacist for advice)

4 **DOAC choice** (consider patient preference and lifestyle- adapt dosing as below); see appendix 1 (counselling), appendix 2 (initiation flowchart for DOAC. In SEL amber 2 on SEL JMF

	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	1 or more of - Weight ≤ 60kg - CrCL 15-50ml/min - On ciclosporin, dronedarone, erythromycin, ketoconazole	CrCL 15-49ml/min	2 or more of : - Age ≥ 80 years - Weight ≤ 60kg - Cr ≥ 133µmol/L OR CrCl 15- 29ml/min	- 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

5 ***Monitoring:*** For patients who DNA for monitoring, refer to practice repeat prescribing protocol

First Review (Ideally after 1 month of therapy)	**Then MINIMUM YEARLY review** (More frequent renal, liver and haemoglobin monitoring if CrCl <60ml/min, age over 75 years and/or frail- see table 6 below)
- **Check for side effects** (*refer to SPC for each DOAC- table 4*) – seek advice and guidance from haematology clinic if present/a concern - **Check for bruising/bleeding** – refer for further investigation according to local pathways as indicated (see DOAC FAQ. For more information) - **U&Es and FBC**- as specified by initiating clinic/secondary care and/or if indicated by a change to clinical state - **Check CrCl** (and review DOAC dosing- *see table 4*) - **Check medication adherence**- refer to community pharmacist for NMS (New Medicines Service) and further support (refer to DOAC counselling checklist- *appendix 1)* - **Schedule repeat prescriptions and review**	- **Age** – check if DOAC dosage adjustment is required (*see table 4)* - **Weight** - check if DOAC dosage adjustment is required (*see table 4*) - **FBC** - investigate any Hb drop without an identifiable cause and if platelets <100 - **LFTs** – seek advice and guidance from haematology clinic if Bilirubin >1.5 ULN, AST/ALT >2 x ULN - **U&Es and CrCL** (*as per table below*)- check if DOAC dosage adjustment is required. - **Interacting/new medications-** check if may effect DOAC dosing and set a review/course length date (seek advice from pharmacist as indicated)

6 ***Renal function monitoring frequency:*** (see also guidance Calculating Renal Function)

Creatinine Clearance (CrCl) range (ml/min)	How often to check renal function?
<15	**All DOACs contraindicated**, refer to specialist (to consider warfarin)
15 to 30	3 monthly, consider referral to specialist (dabigatran contraindicated)
30 to 60 and/or aged >75 years and/or frail±	6 monthly
All patients aged > 75 years and/or frail	4 to 6 monthly ±
>60	12 monthly

±EHRA/ESC 2018: 6 monthly renal, liver function (LFT) and haemoglobin (Hb) monitoring for elderly and frail patients

Appendix 1: DOAC in AF Counselling Checklist for healthcare professionals (HCP)

Apixaban (Eliquis®), Dabigatran (Pradaxa®), Edoxaban (Lixiana®), Rivaroxaban (Xarelto®)

DOAC Agent Counselled: ……..

Counselling points (tailor specifics to your patient and record any queries or concerns in medical notes)	**HCP Sign:**
Explanation of an anticoagulant (increases clotting time and reduces risk of clot formation) **and explanation of atrial fibrillation** (including 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) • Fewer drug interactions	
Name of drug: generic & brand name	
Explanation of dose: strength & frequency	
Duration of therapy: lifelong (unless risk:benefit of anticoagulation changes)	
To take with food (dabigatran and rivaroxaban). Not required for apixaban or edoxaban	
Missed doses: Message is to "take the dose as soon as you remember and then at the same time each day" "Do not take a double dose to make up for the missed dose". For further information: • **Apixaban and dabigatran** can be taken within 6 hours of missed dose, otherwise omit the missed dose • **Edoxaban and rivaroxaban** can be taken within 12 hours of missed dose, otherwise omit the missed dose	
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	
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 managed/reversed by supportive measures and Prothrombin Complex Concentrate (PCC). Antidotes: *Idarucizumab for dabigatran, andexanet alfa for apixaban, rivaroxaban* (SEL JMF)	
Drug interactions and concomitant medication: avoid NSAIDs. Always check with 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's suitable for medication compliance aids if required	
Follow-up appointments, blood tests, and repeat prescriptions: where and when Record here: ……	
Issue relevant patient information AF booklet/leaflet and anticoagulant patient alert card (*For AC alert card supplies* email: pcse.supplies-leeds@nhs.net)	
Give patient opportunity to ask questions and encourage follow up with community pharmacist (NMS – New Medicine Service)	

Appendix 2: Initiation of Anticoagulation (AC) For Stroke Prevention In Non-Valvular Atrial Fibrillation (NVAF)

1) Patient with NVAF diagnosis: discuss risk: benefit of anticoagulant options- NICE recommends a DOAC first line in NVAF considering clinical features, co-morbidities, contra-indications, patient/carer preference and lifestyle (see DOAC FAQs for overprescribing considerations)

⇩

2) Baseline Checks before DOAC Initiation (*see DOAC initiation/monitoring guidance above and calculating renal function for DOACs guidance*)

⇩

3) Following a shared decision with the patient, prescribe a DOAC (see special circumstances table below to guide when to seek specialist advice)
Reduce dose using information on table 4 Criteria for reduced dose in NVAF indication

⇩

4) Patient counselling (*See counselling checklist above*) give patient/carer anticoagulation alert card and product information literature.
Refer to community pharmacist for New Medicines Service (NMS) to support counselling and adherence to DOAC regime

⇩

5) Schedule regular DOAC reviews including adherence checks and dosing adjustments *(see calculating renal function for DOACs guidance, DOAC patient pathway NVAF, FAQs for DOACs guidance)*

Special circumstances	***Recommendation***	***Special circumstances***	***Recommendation***	***Special circumstances***	***Recommendation***
Pregnancy/Breast feeding	*LMWH preferred/ specialist advice*	***Mechanical heart valves*** *(includes tAVI/tAMI, tMVR or MV repair within 3 months)*	*Warfarin/specialist advice- haematology/cardiology*	***Severe renal impairment and/or dialysis (CrCl < 15ml/min)***	*Warfarin/specialist advice*
Active malignancy/ chemotherapy	*Specialist advice*	***Moderate to severe mitral stenosis***	*Warfarin*	***High CrCl >95ml/min***	*Rivaroxaban or apixaban/specialist advice*
HIV antiretrovirals and hepatitis antivirals	*Specialist advice see HIV interactions website- may need therapeutic drug monitoring (TDM)*	***Post coronary event/intervention***	*Cardiology advice: antiplatelet review*	***Antiphospholipid Syndrome (APLS)***	*Specialist advice*
Menorrhagia	*Apixaban/specialist advice*	***Extremes of body weight <50kg and >150kg***	*Specialist advice- usually rivaroxaban or apixaban in obesity*	***On interacting anti-epileptic medication eg carbamazepine, phenytoin***	*Specialist advice- check BNF interactions or SPC for each medication*

References

1. National Institute for Health and Care Excellence . (2023). Clinical Knowledge Summaries . [online] Available at: https://cks.nice.org.uk/topics/atrial-fibrillation/.[cited 07/06/2023]
2. Joint Formulary Committee. British National Formulary (online) Available at: BNF (British National Formulary) | NICE London: BMJ Group and Pharmaceutical Press [cited 07/06/2023]
3. Bristol-Myers Squibb-Pfizer. Summary of Product Characteristics -Eliquis 5 mg film-coated tablets. Last revised 02/2022 [cited 07/06/2023]
4. Boehringer Ingelheim Limited. Summary of Product Characteristics – Pradaxa 150 mg hard capsules. Last revised 09/2022 [cited 07/06/2023]
5. Daiichi Sankyo Europe GmbH. Summary of Product Characteristics – Lixiana 30mg Film-Coated Tablets. Last revised 11/2020 [cited 07/06/2023]
6. Bayer plc. Summary of Product Characteristics – Xarelto 20mg film-coated tablets. Last revised 24/2023 [cited 07/06/2023]
7. MHRA Drug Safety Update. Direct-acting oral anticoagulants (DOACs): reminder of bleeding risk, including availability of reversal agents - GOV.UK (www.gov.uk) [cited 07/06/2023]
8. Southeast London ICB Cardiovascular guidelines. Calculating Renal Function When Monitoring Direct Oral Anticoagulants (DOACs) For Safe and Effective Dosing of Patients. Available at: Calculating-renal-function-for-DOACs-Sept-2019-FINAL.pdf (selondonccg.nhs.uk) [cited 07/06/2023]
9. Guidelines for Medicines Optimisation in Patients with Acute Kidney Injury Guidelines for medicines optimisation in patients with acute kidney injury 2 Guidelines for Medicines Optimisation in Patients with Acute Kidney Injury. (2016). [online] Think Kidney. Available at: https://www.thinkkidneys.nhs.uk/aki/wp-content/uploads/sites/2/2016/03/Guidelines-for-Medicines-optimisation-in-patients-with-AKI-final.pdf. [cited 07/06/2023]
10. Boriani, G., Ruff, C.T., Kuder, J.F., Shi, M., Lanz, H.J., Antman, E.M., Braunwald, E. and Giugliano, R.P. (2020). Edoxaban versus Warfarin in Patients with Atrial Fibrillation at the Extremes of Body Weight: An Analysis from the ENGAGE AF-TIMI 48 Trial. Thrombosis and Haemostasis, 121(02), pp.140–149. doi:https://doi.org/10.1055/s-0040-1716540. [cited 07/06/2023]
11. Southeast London ICB Cardiovascular guidelines. Frequently asked questions (FAQs) concerning Direct Acting Anticoagulants (DOACs) for primary care practitioners in South East London. Available at : https://selondonccg.nhs.uk/wp-content/uploads/dlm_uploads/2021/09/DOAC-FAQs-Sept-2020-FINAL.pdf[cited 07/06/2023]
12. Martin, K.A., Beyer-Westendorf, J., Davidson, B.L., Huisman, M.V., Sandset, P.M. and Moll, S. (2021). Use of direct oral anticoagulants in patients with obesity for treatment and prevention of venous thromboembolism: Updated communication from the ISTH SSC Subcommittee on Control of Anticoagulation. Journal of Thrombosis and Haemostasis, 19(8), pp.1874–1882. doi:https://doi.org/10.1111/jth.15358. [cited 07/06/2023]