NHS
Kent and Medway
Clinical Commissioning Group

Kent and Medway DOAC Monitoring Recommendations for Non-Valvular Atrial Fibrillation (NVAF) in Primary Care

Version 4 (Updated September 2021)

DOCUMENT HISTORY:

Version	Date Updated	Main Changes / Comments
Final Draft	September 2020	Minor changes to wording following comments from ICP MOGs (see under document distribution)
Final Draft V2	September 2020	Following comments from K&M JPC: Part 1 Ongoing monitoring, Line 9: ' as DOAC may need to be stopped' changed to 'as DOAC dose may need to be reduced or alternative treatment initiated'. Approved by JPC
Final Draft V3	September 2020	Approved by Kent and Medway Clinical Cabinet
Version 2 updated May 2021	May 2021	Updated following revisions to NICE Atrial Fibrillation Guidance and NICE CKS Anticoagulation-Oral. Changes to monitoring frequency requirements and recommended bleeding risk tool. Addition of statements re modifiable risk factors and advice if HB dropping. Minor changes to wording. Addition of reference 16.
Version 3 updated Sep 2021	September 2021	Updated following revisions to NICE Atrial Fibrillation Guidance and NICE CKS Anticoagulation-Oral. Comments from JPC on content of document led to wholesale review (Version4)

DOCUMENT DISTRIBUTION

Version	MOG/Clinical Group	Date Agreed	Comments
Draft 3 reformatted	Medway and Swale MOG	Aug 2020	Approved following additional sentence to clarify part 2, point 1, bullet 3.
Draft 3 reformatted	West Kent MOG	Aug 2020	None
Draft 3 reformatted	East Kent MOG (EKPG)	Aug 2020	EKPG- Part 2, point 3, bullet point 6 has been changed from current EK document which gives local advice, to advise to seek specialist advice. Further discussion is required on whether this change is appropriate. PCN and practice pharmacists may need training to be able to provide support. SKC Prescribing Advisor – changes to wording part 2, point 2, bullet 4- "except in situations where a patient's weight is unknown" changed to "in exceptional circumstances where it is

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			not possible to obtain a person's weight".
Draft 3 reformatted	DGS MOG	Aug 2020	No comments from MOG. DVH Cardiology Pharmacist – minor changes to wording. "Tests" changed to "requirements" and added meds initiated by 2^{o} and 3^{0} care and check for interactions to part 1 bullet 6.
Version 4 Draft September 2021	Document was sent to key stakeholders (primary and secondary care specialists) across K&M for comment	Sep 2021	Consultant Haematologist Trust Thrombosis Lead (EKUFT) "A drop in HB of >1g/DL rather than any drop otherwise minor fluctuations will get inappropriate investigations. Check for bleeding" Unless there is a clear cut alternative reason for abnormal LFT. Also consider repeat testing in 4 weeks if mildly abnormal. Investigate for causes as appropriate" K&M Cardiovascular Clinical Lead: Would it be worth including indications (including DVT,PE) and when not use (e.g. metallic valve) etc. or is it out of scope here and best left to GPs? No further comments made
	Document was discussed at length at JPC and KMOCC. The wording in the latest draft reflects the discussion at these committees.	Nov 2021	GP stakeholders requested some rewording around FBC point on table 1 (An Hb drop (>1g/dL) should prompt a review and may require further investigation; consider a clinical assessment of the patient) and LFTs (Caution and seek specialist(s) advice as appropriate when results are out of normal range)

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1. **Monitoring recommendations** for Direct Acting Oral Anticoagulants (DOACS) for patients with **Non-Valvular Atrial Fibrillation (NVAF)** in primary care
2. **Assessing Renal Function for dosing** of DOACs

1. Monitoring Recommendations of Direct Oral Anticoagulants

Baseline Requirements (Before Starting Treatment)

- Baseline clotting screening
- Body weight
- Full blood count
- Liver function tests
- Serum creatinine (for creatinine clearance) · Cockcroft and Gault is recommended for calculating creatinine clearance for DOACs
- Urea and electrolytes

First Review *(ideally after 1 month of therapy)*	**Then MINIMUM YEARLY review for all patients** *(some patients will require more frequent renal, liver and haemoglobin monitoring, see below for details)*
▪ **Check for signs of adverse effects** (*refer to SPC for each DOAC* – seek advice and guidance from haematology clinic if necessary ▪ **Check for bruising/bleeding** – Assess and minimize modifiable risk factors for bleeding: refer for further investigation according to local pathways as indicated ▪ **Assess medication adherence** and reinforce advice regarding regular dosing schedule - refer to community pharmacist for NMS (New Medicines Service) ▪ **Assess for the presence of thromboembolic events.** ▪ **U&Es and FBC**- as specified by initiating clinic/secondary care and/or if indicated by a change to clinical state of patient: **Check CrCl and review DOAC dosing** *(more information in resources linked below)* ▪ **Ask about the use of other medications**, including over-the-counter (OTC) products, to identify possible drug interactions with DOAC. ▪ **Give appropriate information and advice on DOAC treatment.** ▪ **Schedule repeat prescriptions and reviews**	▪ **Age** – check if DOAC dosage adjustment is required ▪ **Actual body weight** - check if DOAC dosage adjustment is required ▪ **FBC** - An Hb drop (>1g/dL) should prompt a review and may require further investigation; consider a clinical assessment of the patient – Check for signs of bleeding and aim to find an identifiable cause. Seek specialist advice as necessary. ▪ **LFTs** – Caution and seek specialist(s) advice as appropriate when results are out of normal range (ALT/ AST over 2 times the upper limit of normal. Total bilirubin over 1.5 times the upper limit of normal[4]); Unless there is a clear cut alternative reason for abnormal LFTs *(refer to SPC links below for further information on individual drugs)* Consider repeat testing in 4 weeks if mildly abnormal. Investigate for causes as appropriate. ▪ **U&Es and CrCl: Check if DOAC dosage adjustment is required** ▪ **Interacting/new medications**- including OTC medicines and medicines initiated by secondary and tertiary care, and check for interactions. Check if interactions effect DOAC dosing and set a review/course length date (seek advice from pharmacist as indicated) ▪ **Review continued need for anticoagulation** and the appropriateness of anticoagulation *(or more frequently if clinically relevant events occur affecting anticoagulation or bleeding risk*) This should include: – An **ORBIT bleeding risk score** *(HAS-BLED score may need to be used until ORBIT has been embedded in clinical pathways and electronic systems)* – **CHA2DS2VASc score** *(For NVAF only)* – ***Document in medical notes***. *(Take into account MHRA advice about bleeding risk and need to monitor renal function in patients with renal impairment)*

Approved by: JPC, KMMOC and Clinical Cabinet
Approval Date: Ratified by Clinical Cabinet December 2021
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For full details of monitoring requirements PRIOR to starting treatment and ONGOING, after treatment has started, please refer to the following resources in the summary table below:

Resource Links:	Apixaban	Rivaroxaban	Edoxaban	Dabigatran
NICE Guidelines (NG196)	Atrial fibrillation: diagnosis and management (for stroke and bleeding risk assessment)			
SPC (Specific Product Characteristics)	Apixaban SPC	Rivaroxaban SPC	Edoxaban SPC	Dabigatran SPC
NICE CKS (Anticoagulation)	Scenario: Apixaban NICE CKS	Scenario: Rivaroxaban NICE CKS	Scenario: Edoxaban NICE CKS	Scenario: Dabigatran NICE CKS
BNF (British National Formulary)	Apixaban	Rivaroxaban	Edoxaban	Dabigatran
SPS (Specialist Pharmacy Service)	1. Direct Acting Oral Anticoagulants (DOACs) in Renal Impairment: Practice Guide to Dosing Issues 2. Monitoring DOACs (Direct Oral Anticoagulants)			
Compliance aid compatibility (As per SPS)	Compatible	Compatible	Compatible	**Not Compatible** *must be kept in original packaging – moisture sensitive*.

Frequency of Monitoring

Patients may need to be monitored more frequently depending on:

- If the person is frail or older than 75 years, monitoring should be repeated every 6 months (as per NICE CKS)
- If the person has a creatinine clearance (CrCl) less than 60 mL/minute, the frequency of monitoring (in months) can be guided by the CrCl divided by 10. For example, every 3 months if CrCl is 30 mL/minute (As per NICE CKS, SPS and European Heart Rhythm association advice)
- If the person has an intercurrent illness that may impact renal or hepatic function, repeat renal and liver function tests as needed ***(Always consider dosing and monitoring frequency in the context of the overall clinical situation)***
- **If renal function has declined, treatment must be reviewed as DOAC dose may need to be reduced or alternative treatment initiated e.g. Warfarin or alternative DOAC. See SPC's for individual anticoagulants (linked in table directly above)**

2. Assessing Renal Function for dosing of DOACs

a) All DOACs are to some extent, dependent on the kidneys for excretion.

b) Using a lower dose, when patients do not meet criteria for dose reduction may increase the risk of embolic events and result in potentially preventable strokes. Using a higher dose than indicated by the renal function may increase the risk of bleeding

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c) Dosage adjustments for DOACs should be based on creatinine clearance (CrCl) estimated using the Cockcroft-Gault (CG) formula (***Note:*** *dose of Apixaban in NVAF is determined by serum creatinine, weight, age as well as CrCl- See BNF)*

The MDCalc Tool is recommended for Calculating Creatinine Clearance (CrCl)

This can be accessed using the link (here) or it can be downloaded as an app.

- MDCalc recognises the need to adjust bodyweight in obese individuals and will calculate a modified estimate of CrCl with a range that is based on ideal body weight, adjusted body weight and actual bodyweight
- *The creatinine clearance calculator on EMIS should only be used in patients with an active prescription for Apixaban, Rivaroxaban or Edoxaban or an issue of the above within the last 3 months, as then it will use actual body weight.*

d) Measure actual body weight each time CrCl is calculated (The Cockcroft and Gault formula may not be accurate for estimation of CrCl at extremes of bodyweight, especially in obese patients. It is important to remember that the CrCl is an estimate and should not be considered in isolation.

e) **Do not use eGFR except in exceptional circumstances where it is not possible to obtain a person's weight** as studies with DOACs have demonstrated that it overestimates renal clearance in comparison with CrCl. Actual body weight and CrCl was used in all the major DOAC clinical trials.

f) In patients at extremes of body weight (<60kg or >120kg) refer to individual drug SPC and seek specialist advice where necessary.

g) After a hospital admission or other transition of care, clinicians should aim to review the dose of a DOAC before issuing a first prescription in primary care. This is because renal function can alter during acute admissions, and it may not have been possible to calculate CrCl during admission.

Further Reading

1) NICE Guidance: Atrial Fibrillation: Diagnosis and Management (NG196). 27th April 2021
2) NICE CKS Anticoagulation– oral.
3) Specialist Pharmacy Service: Direct Acting Oral Anticoagulants (DOACs) in Renal Impairment: Practice Guide to Dosing Issues. Version 3 Feb 2020
4) DOACs (Direct Oral Anticoagulants) monitoring – SPS - Specialist Pharmacy Service – The first stop for professional medicines advice
5) MHRA. DOACs- Reminder of bleeding risk including availability of reversal agents. 29 June 2020.
6) MHRA. Drug Safety Update. Prescribing medicines in renal impairment: using the appropriate estimate of renal function to avoid the risk of adverse drug reactions. 18 October 2019.
7) MHRA/CHM advice: Warfarin and other anticoagulants: monitoring of patients during the COVID-19 pandemic (October 2020)
8) Electronic medicines compendium (summary of product characteristics SPC) for apixaban, dabigatran, edoxaban & rivaroxaban
9) British National Formulary (BNF) summaries for apixaban, dabigatran, edoxaban &rivaroxaban

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