Calculating Renal Function (Creatinine Clearance) When Monitoring Direct Oral Anticoagulants (DOACs) For Safe and Effective Dosing Of Patients in Primary Care In All Indications

The aims of this guidance are to:

a. Ensure that all patients with renal impairment are reviewed at appropriate regular intervals to ensure that they are taking the correct anticoagulant dose
b. Ensure that renal function is monitored consistently during DOAC treatment to provide safe and effective anticoagulation therapy and appropriate dosing according to the patient's indication for anticoagulation

1) How to calculate renal function?

- Use blood results from within the last month and bodyweight (BW) from within the last year (*or more recent if significant weight loss/gain*)
- Use ACTUAL bodyweight to calculate creatinine clearance (CrCl)
- Use the Cockcroft-Gault (CG) equation to estimate CrCl, to reduce the risk of over and under-coagulation
- Primary care systems have inbuilt CrCl calculators- *for EMIS: use actual bodyweight if currently taking a DOAC otherwise use ideal bodyweight (IBW) if actual weight is ≥120kg and for DOAC initiation*
  MD+CALC: Creatinine Clearance (Cockcroft-Gault Equation) (mdcalc.com) (or download MD+CALC app)

Do not use estimated glomerular filtration rate (eGFR) which may overestimate renal clearance, especially in elderly patients with low body weight/ body mass index (BMI)

2) When to seek specialist advice from the local anticoagulation service?

- **extremes of bodyweight < 50kg or > 150kg** as drug level monitoring may be required (*at initiation of treatment and if clinically indicated*)
  NB. When calculating CrCl for these patients: use *adjusted BW* for >120kg and *actual BW* for <50kg unless advised otherwise by anticoagulant clinic
- patients on **dialysis** and **patients with a CrCl <15ml/min** as DOACs are contraindicated in end stage renal impairment
- heart failure patients with fluid overload- use dry weight/ euvolaemic estimate
- patients with extensive amputations, neurological diseases (eg spina bifida, multiple sclerosis) and myopathy that may result in profound muscle loss
- deprescribing considerations: where therapy with a DOAC may no longer be indicated or the patient has made an informed decision to stop the DOAC

3) How often should renal function be monitored?

** more frequent monitoring may be recommended if clinically indicated/advised by specialist or concomitant nephrotoxic medications are prescribed**

Creatinine Clearance (CrCl)	Frequency of Monitoring**
> 60ml/min	Every 12 months
30 to 60ml/min	Every 6 months
All patients aged >75 years and/or frail	Every 4 to 6 months ±
< 30ml/min	At least every 3 months (*dabigatran is contra-indicated*)
<15ml/min	All DOACs are contraindicated – refer to anticoagulation specialist

± EHRA/ESC guidance 2021 recommends 4 to 6 monthly renal, liver function (LFT) and haemoglobin (Hb) monitoring for elderly and frail patients

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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

4) When should the anticoagulant dose be reviewed?

- All patients prescribed a DOAC should be reviewed at least once every 12 months. During the review the DOAC dosing may require amendment as required, according to the indication for anticoagulation, co-prescribed medicines, renal function and other patient- related parameters: refer to drug summary of product characteristics (SPC or BNF) for each DOAC
- This guidance focuses on renal function, but DOAC dose adjustment may also be required with, for example, low body weight, age, interacting medications: please see individual DOAC SPC for further information.

5) What are the recommendations for DOACs in adults with renal impairment? *MHRA 2023*

Severity of renal impairment	**Edoxaban**	**Rivaroxaban**	**Apixaban**	**Dabigatran**
End stage CrCl <15ml/min	Not recommended	Not recommended	Not recommended	Contraindicated
Severe (CrCl 15 to 29ml/min)	NB. for edoxaban moderate to severe renal impairment is defined as CrCl 15 to 50ml/min: **Dose reduction to 30mg daily recommended in all indications**	Use with caution in all indications. **Dose adjustment is recommended in SPAF (15mg daily)** and a specialist may consider in VTE	Use with caution in VTE. **Dose reduction is recommended in SPAF (2.5mg twice daily)**	Contraindicated
Moderate (CrCl 30 to 49ml/min)		**Dose adjustment recommended in SPAF (15mg daily)** and a specialist may consider in VTE	Dose reduction is required in SPAF in some patients **(serum Cr ≥1.5mg/dL or 133 micromole/L associated with age 80 years or older or body weight 60kg or lower**)	**Dose adjustment should be considered** in SPAF and VTE
Mild (CrCl 50 to 80ml/min)	No dose adjustment required (60mg daily) * *caution CrCl >95ml/min*	No dose adjustment required (20mg daily)	Dose reduction is required in SPAF in some patients (*as per above criteria*)	No dose adjustment required (*other dosing criteria may apply e.g. age, "bleed risk"*)

SPAF= prevention of stroke and systemic embolism in patients with non-valvular atrial fibrillation; VTE= treatment of deep vein thrombosis and pulmonary embolism

*For patients with non-valvular atrial fibrillation (NVAF) and high creatinine clearance, in clinical trials there was a trend towards decreasing efficacy with increasing creatinine clearance observed for edoxaban versus well-managed warfarin, therefore edoxaban should be used in patients with NVAF and high CrCl only after a careful evaluation of the individual thromboembolic and bleeding risk. In SEL guidance and the SPC for edoxaban this caution may be considered for patients with CrCl >95ml/min.

Further information:

- **MHRA Drug Safety Update, 25 May 2023: Direct-acting oral anticoagulants (DOACs): reminder of dose adjustments in patients with renal impairment**: https://www.gov.uk/drug-safety-update/direct-acting-oral-anticoagulants-doacs-paediatric-formulations-reminder-of-dose-adjustments-in-patients-with-renal-impairment
- Specialist Pharmacy Service: DOAC monitoring July 2022: https://www.sps.nhs.uk/monitorings/doacs-direct-oral-anticoagulants-monitoring/
- Specialist Pharmacy service: DOACs in renal impairment: Practice guide to dosing issues July 2019; www.sps.nhs.uk
- https://www.anticoagulationuk.org/admin/resources/downloads/dosing-of-direct-oral-anticoagulants-doacs-in-renal-impairement.pdf
- 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.
- Steffel J, Collins R et al; 2021 European Heart Rhythm Association Practical Guide on the use of non-vitamin K antagonist oral anticoagulants in patients with atrial fibrillation; Europace (2021) 23, 1612-1676 https://www.escardio.org/Guidelines/Recommended-Reading/Heart-Rhythm/Novel-Oral-Anticoagulants-for-Atrial-Fibrillation