

MHRA

Drug Safety Update

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MHRA
Regulating Medicines and Medical Devices

Direct-acting oral anticoagulants (DOACs) Reminder of dose adjustments in patients with renal impairment

Exposure to DOACs is increased in patients with renal impairment and it is therefore important that patients receive an appropriate dose adjusted for renal function.

Renal function in adults should be assessed by calculating creatinine clearance (CrCl) using the Cockcroft-Gault formula. See BNF resources on [Prescribing in renal impairment](#). Patients with renal impairment should be reviewed regularly to ensure ongoing efficacy and safety, with dosing adjusted as required.

Recommendations for use of DOACs in patients with renal impairment were published in the [June 2020 issue of Drug Safety Update](#). Following queries from healthcare professionals, the MHRA has updated the table below for adults, which provides further clarity on dose adjustment in various indications and in patients with different severities of renal impairment.

Table 1 - Recommendations for DOACs in adults with renal impairment

Severity of renal impairment (creatinine clearance (CrCl))	Dabigatran	Apixaban	Edoxaban	Rivaroxaban
End stage (CrCl less than 15 mL per minute)	Contraindicated	Not recommended	Not recommended	Not recommended
Severe (CrCl 15 to 29 mL per minute)**	Contraindicated	To be used with caution in VTEp and VTEt; dose reduction is recommended in SPAF	Dose reduction recommended in all indications	Use with caution in all indications Dose adjustment is recommended in SPAF and should be considered in VTEt
Moderate (CrCl 30 to 49 mL per minute)**	Dose adjustment recommended in VTEp and should be considered in SPAF and VTEt	Dose reduction is required in SPAF in some patients*	Dose reduction recommended in all indications	Dose adjustment recommended in SPAF and should be considered in VTEt
Mild (CrCl 50 to 80 mL per minute)**	No dose adjustment required	Dose reduction is required in SPAF in some patients*	No dose adjustment required***	No dose adjustment required

CrCl = creatinine clearance. SPAF = prevention of stroke and systemic embolism in patients with non-valvular atrial fibrillation (NVAF). VTEp = prevention of VTE (venous thromboembolism) in elective hip or knee replacement surgery. VTEt = treatment of deep vein thrombosis and pulmonary embolism, and prevention of recurrent VTE events.

*In patients with serum creatinine ≥ 1.5 mg/dL (133 micromole/L) associated with age 80 years or older or body weight 60kg or lower. **For edoxaban moderate to severe renal impairment is defined as CrCl 15 to 50 mL/min. ***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.

Advice for healthcare professionals:

- ensure all patients with renal impairment receive an appropriate DOAC dose and monitor renal function during treatment to ensure dose remains appropriate
- report suspected adverse drug reactions associated with DOACs on a Yellow Card, including thromboembolic or haemorrhagic events
- all patients with renal impairment who are taking DOACs will be reviewed regularly to make sure they are taking the correct dose