Anticoagulation Considerations and Dose Adjustments in Chronic Kidney Disease

CME OUTFITTERS

Adapted from Aursulesei V, Costache II. Anticoagulation in chronic kidney disease: from guidelines to clinical practice. *Clin Cardiol*. 2019;42(8):774–782.

Pharmacokinetic Properties of Oral Anticoagulants

ORAL ANTICOAGULANT	MECHANISM OF ACTION	PRODRUG	PHARMACOKINETIC PROPERTIES		
			Metabolism	Dialyzable	Dose Adjustment
Warfarin	Vitamin K antagonist	No	Predominantly via cytochrome P450 type 2C9 (CYP2C9)	No	No
Dabigatran	Direct inhibitor of free thrombin and fibrin-bound thrombin	Yes	Renal excretion 80%	Yes	Yes
Rivaroxaban	Free and clot-bound Xa factor inhibitor, prothrombinase activity inhibitor	No	Renal excretion 66%, 36% as unchanged drug	No	Yes
Apixaban	Free and clot-bound Xa factor inhibitor	No	Metabolized in liver via CYP3A4, renal excretion 27% and in feces	Partial	No
Edoxaban	Free Xa factor and tissue factor inhibitor	No	10% hydrolyzed by carboxylesterase 1, 50% unchanged upon renal excretion	No	Yes

Table adapted from: Jain N, Reilly RF. Clinical pharmacology of oral anticoagulants in patients with kidney disease. *Clin J Am Soc Nephrol*. 2019;14(2):278–287. Lutz J, Jurk K, Schinze H, et al. Direct oral anticoagulants in patients with chronic kidney disease: patient selection and special considerations. *Int J Nephrol Renovasc Dis*. 2017;10:135–143.

Dose Adjustment for DOACs According to Chronic Kidney Disease Severity in Patients with Atrial Fibrillation/Venous Thromboembolism

Recommended Oral Anticoagulant	CrCl (mL/min) Estimated Using the Cockroft-Gault Equation				
	≥50	30–49	15–29	<15	ESRD on Dialysis
	DOACs	DOACs	Warfarin/DOACs	Warfarin/DOACs (with caution)	
Warfarin	Preferable to adjust the dose function of time in therapeutic range, optimal ≥70%				
Dabigatran	150 mg twice daily 110 mg twice daily ≥80 years, or associated with P-glycoprotein inhibitors, or high risk of hemorrhage	Idem	The United States (based only on FDA approval)—75 mg twice daily Europe—NO	No	
Rivaroxaban	20 mg once daily	15 mg once daily (dose used by landmark trials recommended by small pharmacokinetic studies)		No	
Apixaban	5 mg twice daily 2.5 mg twice daily if any ≥2 of the following: age ≥80 years, body weight ≤60 kg and creatinine ≥1.5 mg/dL	Idem	2.5 mg twice daily	The United States—2.5 mg twice daily Europe—NO	The United States (FDA)—5 mg twice daily Europe—NO
Edoxaban	60 mg once daily 30 mg once daily when ≥2 of the following criteria are met: body weight ≤60 kg, CrCl 30–50 mL/min and therapy with verapamil, dronedarone, or quinidine is associated FDA black box warning for CrCl >95 mL/min	30 mg once daily		No	

Abbreviations: CrCl, creatinine clearance; DOAC, direct oral anticoagulant; ESRD, end-stage renal disease; FDA, Food and Drug Administration.

Table adapted from: Potpara TS, Ferro CJ, Lip GYH. Use of oral anticoagulants in patients with atrial fibrillation and renal dysfunction. *Nat Rev*. 2018;14:337–351. Harel Z, Sholzberg M, Shah PS, et al. Comparisons between novel oral anticoagulants and vitamin K antagonists in patients with CKD. *J Am Soc Nephrol*. 2014;25:431–442. Bhatia HS, Hsu JC, Kim RK. Atrial fibrillation and chronic kidney disease: a review of options for therapeutic anticoagulation to reduce thromboembolism risk. *Clin Cardiol*. 2018;41:1395–1402. Ghadban R, Flaker G, Katta N, Alpert MA. Anti-thrombotic therapy for atrial fibrillation in patients with chronic kidney disease: current views. *Hemodial Int*. 2017;21:S47–S56.