Drug-Drug Interaction Guide: From HIV Prevention to Treatment





Table 22: Anticoagulants (also see prescribing information)			
→ Warfarin, non-VKA oral anticoagulants (NOACs), low molecular weight heparins (LMWHs)			
Class or Drug	Mechanism of Action	Clinical Comments	
 NRTIs Dolutegravir (DTG) Bictegravir (BIC) Cabotegravir (CAB) Raltegravir (RAL) Rilpivirine (RPV) Doravirine (DOR) 	No significant interactions are expected.	No dose adjustments are necessary.	
Elvitegravir (EVG), boosted	Warfarin: Metabolism of warfarin could potentially decrease (or more rarely) increase. Rivaroxaban, dabigatran, apixaban: Concentrations may increase, increasing bleeding risk. LMWHs: No significant interactions are expected.	 Warfarin: Use cautiously with warfarin; if use is necessary, increase INR monitoring. If INR increases, decrease warfarin dose. If INR decreases, increase warfarin dose slowly. Rivaroxaban: Do not coadminister. Apixaban: Reduce apixaban dose to 2.5 mg twice per day; if patient is already taking 2.5 mg twice per day, avoid concomitant use. Dabigatran: In patients with good renal function, no dose adjustments are necessary. In patients with moderate to severe renal dysfunction, do not use this combination. Consider switching to another ARV regimen without booster to avoid interaction. Edoxaban: For stroke prevention in patients with nonvalvular atrial fibrillation: No dose adjustments are necessary. For patients with DVT and PE: Administer edoxaban 30 mg once daily. LMWHs: No dose adjustments are necessary. 	
Boosted PIs	 Warfarin: Metabolism of warfarin could potentially decrease (or more rarely) increase. Rivaroxaban, dabigatran, apixaban: Concentrations may increase, increasing bleeding risk. LMWHs: No significant interactions are expected. 	 Avoid concomitant use or use lowest effective dose of factor Xa inhibitor to avoid increased bleeding risk. Warfarin: Use cautiously with warfarin; if use is necessary, increase INR monitoring. If INR increases, decrease warfarin dose. If INR decreases, increase warfarin dose slowly. Rivaroxaban: Do not coadminister. 	



Table 22: Anticoagulants (also see prescribing information) → Warfarin, non-VKA oral anticoagulants (NOACs), low molecular weight heparins (LMWHs)		
		 Apixaban: Reduce apixaban dose to 2.5 mg twice per day; if patient is already taking 2.5 mg twice per day, avoid concomitant use.
		Dabigatran:
		 Separate doses of dabigatran and boosted PIs by at least 2 hours.
		 RTV boosting of PIs may be safer than COBI boosting with concomitant dabigatran [Kakadiya, et al. 2018]. Avoid dabigatran in patients with renal impairment (CrCl <50 mL/min) who are taking boosted PIs.
		• Edoxaban:
		 For stroke prevention in patients with nonvalvular atrial fibrillation: No dose adjustments are necessary. For DVT and PE: Administer edoxaban 30 mg once daily.
		LMWHs: No dose adjustments are necessary.
Efavirenz (EFV)Etravirine (ETR)	 Warfarin: Metabolism of warfarin could potentially increase (or more rarely) decrease). 	 Use cautiously with warfarin; if use is necessary, increase INR monitoring.
Nevirapine (NVP)	 NOACs, LMWHs: EFV may reduce levels of NOACs metabolized via CYP3A4. 	If INR increases, decrease warfarin dose.If INR decreases, increase warfarin dose slowly.
		 NOACs, LMWHs: Avoid NOACs with EFV and NVP; use alternative HIV regimen.
Lenacapavir (LEN)	DOAC levels potentially increase due to effect on CYP3A4 and P-gP.	No dose adjustment needed; monitor for increased risk of bleeding.
		Refer to DOAC prescribing information for use with moderate CYP3A4 and P-gP inhibitors.

Abbreviations: ARV, antiretroviral; COBI, cobicistat; CrCl, creatinine clearance; CYP, cytochrome P450; DOAC, direct oral anticoagulant; DVT, deep vein thrombosis; INR, international normalized ratio; NRTI, nucleoside reverse transcriptase inhibitor; PE, pulmonary embolism; P-gP, P-glycoprotein; PI, protease inhibitor; RTV, ritonavir.

Reference

Kakadiya PP, Higginson RT, Fulco PP. Ritonavir-boosted protease inhibitors but not cobicistat appear safe in HIV-positive patients ingesting dabigatran. *Antimicrob Agents Chemother* 2018;62(2):e02275-02217. [PMID: 29133562] https://pubmed.ncbi.nlm.nih.gov/29133562