Resource: ART Drug-Drug Interactions

August 2024

Table 22: Anticoagulants (also see drug package inserts)		
→ 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.

Table 22: Anticoagulants (also see drug package inserts)		
→ Warfarin, non-VKA oral anticoagulants (NOACs), low molecular weight heparins (LMWHs)		
Class or Drug	**Mechanism of Action**	**Clinical Comments**
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. • **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) • Nevirapine (NVP)	• **Warfarin:** Metabolism of warfarin could potentially increase (or more rarely) decrease). • **NOACs, LMWHs:** EFV may reduce levels of NOACs metabolized via CYP3A4.	• Use cautiously with warfarin; if use is necessary, increase INR monitoring. – 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):e02275-17. [PMID: 29133562] https://pubmed.ncbi.nlm.nih.gov/29133562