



## Resource: ART Drug-Drug Interactions

April 2023

Table 21: 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
<ul style="list-style-type: none"> <li>• NRTIs</li> <li>• Dolutegravir (DTG)</li> <li>• Bictegravir (BIC)</li> <li>• Cabotegravir (CAB)</li> <li>• Raltegravir (RAL)</li> <li>• Rilpivirine (RPV)</li> <li>• Doravirine (DOR)</li> </ul>	No significant interactions are expected.	No dose adjustments are necessary.
Elvitegravir (EVG), boosted	<ul style="list-style-type: none"> <li>• <b>Warfarin:</b> Metabolism of warfarin could potentially decrease (or more rarely) increase.</li> <li>• <b>Rivaroxaban, dabigatran, apixaban:</b> Concentrations may increase, increasing bleeding risk.</li> <li>• <b>LMWHs:</b> No significant interactions are expected.</li> </ul>	<ul style="list-style-type: none"> <li>• <b>Warfarin:</b> Use cautiously with warfarin; if use is necessary, increase INR monitoring.               <ul style="list-style-type: none"> <li>– If INR increases, decrease warfarin dose.</li> <li>– If INR decreases, increase warfarin dose slowly.</li> </ul> </li> <li>• <b>Rivaroxaban:</b> Do not coadminister.</li> <li>• <b>Apixaban:</b> Reduce apixaban dose to 2.5 mg twice per day; if patient is already taking 2.5 mg twice per day, avoid concomitant use.</li> <li>• <b>Dabigatran:</b> <ul style="list-style-type: none"> <li>– In patients with good renal function, no dose adjustments are necessary.</li> <li>– In patients with moderate to severe renal dysfunction, do not use this combination.</li> <li>– Consider switching to another ARV regimen without booster to avoid interaction.</li> </ul> </li> <li>• <b>Edoxaban:</b> <ul style="list-style-type: none"> <li>– For stroke prevention in patients with nonvalvular atrial fibrillation: No dose adjustments are necessary.</li> <li>– For patients with DVT and PE: Administer edoxaban 30 mg once daily.</li> </ul> </li> <li>• <b>LMWHs:</b> No dose adjustments are necessary.</li> </ul>

**Table 21: 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	<ul style="list-style-type: none"> <li>• <b>Warfarin:</b> Metabolism of warfarin could potentially decrease (or more rarely) increase.</li> <li>• <b>Rivaroxaban, dabigatran, apixaban:</b> Concentrations may increase, increasing bleeding risk.</li> <li>• <b>LMWHs:</b> No significant interactions are expected.</li> </ul>	<ul style="list-style-type: none"> <li>• <b>Avoid concomitant use</b> or use lowest effective dose of factor Xa inhibitor to avoid increased bleeding risk.</li> <li>• <b>Warfarin:</b> Use cautiously with warfarin; if use is necessary, increase INR monitoring.               <ul style="list-style-type: none"> <li>– If INR increases, decrease warfarin dose.</li> <li>– If INR decreases, increase warfarin dose slowly.</li> </ul> </li> <li>• <b>Rivaroxaban:</b> Do not coadminister.</li> <li>• <b>Apixaban:</b> Reduce apixaban dose to 2.5 mg twice per day; if patient is already taking 2.5 mg twice per day, avoid concomitant use.</li> <li>• <b>Dabigatran:</b> <ul style="list-style-type: none"> <li>– Separate doses of dabigatran and boosted PIs by at least 2 hours.</li> <li>– RTV boosting of PIs may be safer than COBI boosting with concomitant dabigatran [Kakadiya, et al. 2018].</li> <li>– Avoid dabigatran in patients with renal impairment (CrCl &lt;50 mL/min) who are taking boosted PIs.</li> </ul> </li> <li>• <b>Edoxaban:</b> <ul style="list-style-type: none"> <li>– For stroke prevention in patients with nonvalvular atrial fibrillation: No dose adjustments are necessary.</li> <li>– For DVT and PE: Administer edoxaban 30 mg once daily.</li> </ul> </li> <li>• <b>LMWHs:</b> No dose adjustments are necessary.</li> </ul>
<ul style="list-style-type: none"> <li>• Efavirenz (EFV)</li> <li>• Etravirine (ETR)</li> <li>• Nevirapine (NVP)</li> </ul>	<ul style="list-style-type: none"> <li>• <b>Warfarin:</b> Metabolism of warfarin could potentially increase (or more rarely) decrease).</li> <li>• <b>NOACs, LMWHs:</b> EFV may reduce levels of NOACs metabolized via CYP3A4.</li> </ul>	<ul style="list-style-type: none"> <li>• Use cautiously with warfarin; if use is necessary, increase INR monitoring.               <ul style="list-style-type: none"> <li>– If INR increases, decrease warfarin dose.</li> <li>– If INR decreases, increase warfarin dose slowly.</li> </ul> </li> <li>• <b>NOACs, LMWHs:</b> Avoid NOACs with EFV and NVP; use alternative HIV regimen.</li> </ul>
Lenacapavir (LEN)	DOAC levels potentially increase due to effect on CYP3A4 and P-gP.	<ul style="list-style-type: none"> <li>• No dose adjustment needed; monitor for increased risk of bleeding.</li> <li>• Refer to DOAC prescribing information for use with moderate CYP3A4 and P-gP inhibitors.</li> </ul>

**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). [PMID: 29133562] <https://pubmed.ncbi.nlm.nih.gov/29133562>