



## Resource: ART Drug-Drug Interactions

April 2023

Table 36: Opioid Analgesics and Tramadol (also see drug package inserts)		
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>• Etravirine (ETR)</li> <li>• Doravirine (DOR)</li> <li>• Fostemsavir (FTR)</li> </ul>	No significant interactions reported.	No dose adjustments are required.
Elvitegravir (EVG), boosted	<ul style="list-style-type: none"> <li>• <b>Opioid analgesics:</b> Complex mechanisms of metabolism and formation of both active and inactive metabolites create interactions of unclear significance between these drugs and boosted EVG.</li> <li>• <b>Tramadol:</b> Tramadol exposure is increased with CYP3A inhibition, but this reduces conversion to more potent active metabolite seen when tramadol is metabolized by CYP2D6.</li> </ul>	<ul style="list-style-type: none"> <li>• <b>Opioid analgesics:</b> Monitor for signs of opiate toxicity and analgesic effect and dose these analgesics accordingly.</li> <li>• <b>Tramadol:</b> When tramadol is given with COBI or RTV, monitoring for tramadol-related adverse effects and analgesic effect may be required as clinically indicated; adjust tramadol dosage if needed.</li> </ul>
Boosted PIs	<ul style="list-style-type: none"> <li>• <b>Opioid analgesics:</b> Complex mechanisms of metabolism and formation of both active and inactive metabolites create interactions of unclear significance between these drugs and boosted PIs.</li> <li>• <b>Tramadol:</b> Tramadol exposure is increased with CYP3A inhibition, but this reduces conversion to more potent active metabolite seen when tramadol is metabolized by CYP2D6.</li> </ul>	<ul style="list-style-type: none"> <li>• <b>Opioid analgesics:</b> Monitor for signs of opiate toxicity and analgesic effect; dose these analgesics accordingly.</li> <li>• <b>Tramadol:</b> When tramadol is given with COBI or RTV, monitoring for tramadol-related adverse effects and analgesic effect may be required as clinically indicated; adjust tramadol dosage if needed.</li> </ul>
Efavirenz (EFV)	<ul style="list-style-type: none"> <li>• <b>Morphine, hydromorphone:</b> Metabolism could be reduced by EFV.</li> <li>• <b>Oxycodone</b> may be metabolized faster to inactive metabolite by EFV.</li> <li>• <b>Meperidine:</b> Coadministration can potentially increase amount of neurotoxic metabolite, thereby increasing seizure risk.</li> <li>• <b>Tramadol:</b> EFV may reduce tramadol concentration without affecting pathway that increases development of more potent active metabolites.</li> </ul>	<ul style="list-style-type: none"> <li>• <b>Morphine, hydromorphone:</b> Monitor for signs of opiate toxicity when using with EFV.</li> <li>• <b>Oxycodone:</b> Dose adjustment of oxycodone may be required when dosing with EFV.</li> <li>• <b>Meperidine:</b> If possible, avoid concomitant use; use alternative opiate pain medication or ARV.</li> <li>• <b>Tramadol:</b> When given with tramadol, a priori dose adjustments are necessary.</li> </ul>

<b>Table 36: Opioid Analgesics and Tramadol</b> (also see drug package inserts)		
<b>Class or Drug</b>	<b>Mechanism of Action</b>	<b>Clinical Comments</b>
Lenacapavir (LEN)	Moderate inhibition of CYP3A4 potentially increases opioid levels.	<ul style="list-style-type: none"> <li>• Monitor for therapeutic effects and adverse reactions associated with CYP3A-metabolized opioid analgesics, including potentially fatal respiratory depression.</li> <li>• <b>Tramadol:</b> Consider tramadol dose reduction with concomitant use.</li> </ul>
<b>Abbreviations:</b> ARV, antiretroviral; COBI, cobicistat; CYP, cytochrome P450; NRTI, nucleoside reverse transcriptase inhibitor; PI, protease inhibitor; RTV, ritonavir.		