Resource: ART Drug-Drug Interactions

August 2024

Table 37: Opioid Analgesics and Tramadol (also see drug package inserts)		
Class or Drug	Mechanism of Action	Clinical Comments
 NRTIs Dolutegravir (DTG) Bictegravir (BIC) Cabotegravir (CAB) Raltegravir (RAL) Rilpivirine (RPV) Etravirine (ETR) Doravirine (DOR) Fostemsavir (FTR) 	No significant interactions reported.	No dose adjustments are required.
Elvitegravir (EVG), boosted	 Opioid analgesics: Complex mechanisms of metabolism and formation of both active and inactive metabolites create interactions of unclear significance between these drugs and boosted EVG. Tramadol: Tramadol exposure is increased with CYP3A inhibition, but this reduces conversion to more potent active metabolite seen when tramadol is metabolized by CYP2D6. 	 Opioid analgesics: Monitor for signs of opiate toxicity and analgesic effect and dose these analgesics accordingly. Tramadol: 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.
Boosted PIs	 Opioid analgesics: Complex mechanisms of metabolism and formation of both active and inactive metabolites create interactions of unclear significance between these drugs and boosted PIs. Tramadol: Tramadol exposure is increased with CYP3A inhibition, but this reduces conversion to more potent active metabolite seen when tramadol is metabolized by CYP2D6. 	 Opioid analgesics: Monitor for signs of opiate toxicity and analgesic effect; dose these analgesics accordingly. Tramadol: 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.
Efavirenz (EFV)	 Morphine, hydromorphone: Metabolism could be reduced by EFV. Oxycodone may be metabolized faster to inactive metabolite by EFV. Meperidine: Coadministration can potentially increase amount of neurotoxic metabolite, thereby increasing seizure risk. Tramadol: EFV may reduce tramadol concentration without affecting pathway that increases development of more potent active metabolites. 	 Morphine, hydromorphone: Monitor for signs of opiate toxicity when using with EFV. Oxycodone: Dose adjustment of oxycodone may be required when dosing with EFV. Meperidine: If possible, avoid concomitant use; use alternative opiate pain medication or ARV. Tramadol: When given with tramadol, a priori dose adjustments are necessary.

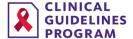


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Lenacapavir (LEN)	Moderate inhibition of CYP3A4 potentially increases opioid levels.	 Monitor for therapeutic effects and adverse reactions associated with CYP3A-metabolized opioid analgesics, including potentially fatal respiratory depression. Tramadol: Consider tramadol dose reduction with concomitanuse.

Abbreviations: ARV, antiretroviral; COBI, cobicistat; CYP, cytochrome P450; NRTI, nucleoside reverse transcriptase inhibitor; PI, protease inhibitor; RTV, ritonavir.