

Table 37: Opioid Analgesics and Tramadol (also see prescribing information)		
Class or Drug	Mechanism of Action	Clinical Comments
<ul style="list-style-type: none"> • 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	<ul style="list-style-type: none"> • 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. 	<ul style="list-style-type: none"> • 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	<ul style="list-style-type: none"> • 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. 	<ul style="list-style-type: none"> • 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)	<ul style="list-style-type: none"> • 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. 	<ul style="list-style-type: none"> • 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.
Lenacapavir (LEN)	Moderate inhibition of CYP3A4 potentially increases opioid levels.	<ul style="list-style-type: none"> • Monitor for therapeutic effects and adverse reactions associated with CYP3A-metabolized opioid analgesics, including potentially fatal respiratory depression. • Tramadol: Consider tramadol dose reduction with concomitant use.

Table 37: Opioid Analgesics and Tramadol (also see prescribing information)		
Class or Drug	Mechanism of Action	Clinical Comments
Abbreviations: ARV, antiretroviral; COBI, cobicistat; CYP, cytochrome P450; NRTI, nucleoside reverse transcriptase inhibitor; PI, protease inhibitor; RTV, ritonavir.		