



## Resource: ART Drug-Drug Interactions

April 2023

Table 42: Methadone, Buprenorphine (BUP), Naloxone (NLX), and Naltrexone [a] (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>• Elvitegravir (EVG), boosted</li> <li>• Doravirine (DOR)</li> <li>• Fostemsavir (FTR)</li> </ul>	<b>BUP, methadone:</b> No significant are interactions expected.	No dose adjustments are necessary.
Atazanavir (ATV), unboosted	<ul style="list-style-type: none"> <li>• <b>BUP, norbuprenorphine:</b> ATV greatly increases BUP and norbuprenorphine concentrations; may decrease ATV concentrations.</li> <li>• <b>Methadone:</b> No significant interactions are expected.</li> </ul>	<ul style="list-style-type: none"> <li>• <b>BUP:</b> Coadministration is not recommended; RTV boosting may decrease effect.</li> <li>• <b>Methadone:</b> No dose adjustments are required; exercise caution because both drugs may increase QT prolongation.</li> </ul>
Ritonavir (RTV)-boosted PIs	<b>BUP:</b> RTV-boosted PIs may greatly increase BUP concentrations, but clinical significance of this is unknown because BUP dosing is based on <a href="#">Clinical Opiate Withdrawal Scale</a> .	<b>BUP:</b> When administering with RTV-boosted PIs, monitor for signs of increased opioid toxicity, including sedation, impaired cognition, and respiratory distress.
Cobicistat (COBI)-boosted PIs	<ul style="list-style-type: none"> <li>• <b>BUP/NLX:</b> COBI-boosted PIs may increase BUP concentrations while decreasing NLX concentrations when given with sublingual BUP/NLX.</li> <li>• <b>Methadone:</b> COBI does not appear to have any significant effect on methadone concentration.</li> </ul>	<ul style="list-style-type: none"> <li>• <b>BUP, BUP/NLX:</b> When administering with COBI-boosted PIs, titrate carefully to achieve clinical effect.</li> <li>• <b>Methadone:</b> Based on efficacy and safety, initiate at lowest possible dose and titrate to achieve clinical effect; monitor for signs and symptoms of opiate withdrawal.</li> </ul>
RTV-boosted darunavir (DRV), taken twice per day	<ul style="list-style-type: none"> <li>• <b>BUP, BUP/NLX:</b> Combination has no effect on BUP/NLX concentrations.</li> <li>• <b>Methadone:</b> RTV-boosted DRV taken twice per day may reduce methadone concentrations.</li> </ul>	<b>Methadone:</b> Monitor for signs of opiate withdrawal and increase methadone dose if necessary.
Rilpivirine (RPV)	<ul style="list-style-type: none"> <li>• <b>BUP:</b> No significant interactions are expected.</li> <li>• <b>Methadone:</b> RPV mildly reduces methadone concentrations.</li> </ul>	<ul style="list-style-type: none"> <li>• <b>Methadone:</b> Monitor for signs of methadone withdrawal; increase dose as necessary.</li> <li>• <b>Methadone, BUP:</b> Use cautiously with RPV; supratherapeutic doses of RPV have been known to cause increase in QT prolongation.</li> </ul>

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<b>Class or Drug</b>	<b>Mechanism of Action</b>	<b>Clinical Comments</b>
Efavirenz (EFV)	<ul style="list-style-type: none"> <li>• <b>BUP:</b> When given with BUP (monotherapy), EFV significantly reduces BUP concentrations, but no patients developed opioid withdrawal.</li> <li>• <b>Methadone:</b> EFV induces methadone metabolism via CYP3A4 and reduces methadone concentrations.</li> </ul>	<ul style="list-style-type: none"> <li>• <b>BUP:</b> When given with BUP, dose adjustments are unlikely to be required, but monitor for withdrawal symptoms. If withdrawal symptoms occur, increase BUP dose accordingly.</li> <li>• <b>Methadone:</b> Titrate to achieve clinical effect; monitor for signs and symptoms of opioid withdrawal.</li> </ul>
Etravirine (ETR)	<ul style="list-style-type: none"> <li>• <b>BUP:</b> No significant interactions are expected.</li> <li>• <b>Methadone:</b> ETR may slightly increase methadone concentrations.</li> </ul>	<ul style="list-style-type: none"> <li>• <b>BUP, methadone:</b> Titrate opioid or antagonist as required to achieve clinical effect; monitor for signs of withdrawal or opioid toxicity.</li> <li>• <b>Methadone:</b> Monitor for signs of methadone toxicity and reduce dose if necessary.</li> </ul>
Lenacapavir (LEN)	<b>Methadone, BUP:</b> Moderate inhibition of CYP3A4 and P-gP potentially increases methadone or BUP levels.	<ul style="list-style-type: none"> <li>• <b>Patients initiating MAT while already on LEN:</b> Initiate MAT at lowest initial or maintenance dose.</li> <li>• <b>Patients initiating LEN while already on MAT:</b> MAT dose adjustments may be needed.</li> <li>• Monitor for excess sedation and/or respiratory depression.</li> </ul>
<p><b>Abbreviations:</b> ARV, antiretroviral; CYP, cytochrome P450; MAT, medication-assisted therapy; NRTI, nucleoside reverse transcriptase inhibitor; P-gP, P-glycoprotein; PI, protease inhibitor.</p> <p><b>Note:</b></p> <p>a. No significant interactions are expected between ARVs, naloxone, and naltrexone.</p>		