Table 43: Methadone, Buprenorphine (BUP), Naloxone (NLX), and Naltrexone [a] (also see prescribing information)		
Class or Drug	**Mechanism of Action**	**Clinical Comments**
• NRTIs • Dolutegravir (DTG) • Bictegravir (BIC) • Cabotegravir (CAB) • Raltegravir (RAL) • Elvitegravir (EVG), boosted • Doravirine (DOR) • Fostemsavir (FTR)	**BUP, methadone:** No significant interactions are expected.	No dose adjustments are necessary.
Atazanavir (ATV), unboosted	• **BUP, norbuprenorphine:** ATV greatly increases BUP and norbuprenorphine concentrations; may decrease ATV concentrations. • **Methadone:** No significant interactions are expected.	• **BUP:** Coadministration is not recommended; RTV boosting may decrease effect. • **Methadone:** No dose adjustments are required; exercise caution because both drugs may increase QT prolongation.
Ritonavir (RTV)-boosted PIs	**BUP:** RTV-boosted PIs may greatly increase BUP concentrations, but clinical significance of this is unknown because BUP dosing is based on Clinical Opiate Withdrawal Scale.	**BUP:** When administering with RTV-boosted PIs, monitor for signs of increased opioid toxicity, including sedation, impaired cognition, and respiratory distress.
Cobicistat (COBI)-boosted PIs	• **BUP/NLX:** COBI-boosted PIs may increase BUP concentrations while decreasing NLX concentrations when given with sublingual BUP/NLX. • **Methadone:** COBI does not appear to have any significant effect on methadone concentration.	• **BUP, BUP/NLX:** When administering with COBI-boosted PIs, titrate carefully to achieve clinical effect. • **Methadone:** Based on efficacy and safety, initiate at lowest possible dose and titrate to achieve clinical effect; monitor for signs and symptoms of opiate withdrawal.
RTV-boosted darunavir (DRV), taken twice per day	• **BUP, BUP/NLX:** Combination has no effect on BUP/NLX concentrations. • **Methadone:** RTV-boosted DRV taken twice per day may reduce methadone concentrations.	**Methadone:** Monitor for signs of opiate withdrawal and increase methadone dose if necessary.
Rilpivirine (RPV)	• **BUP:** No significant interactions are expected. • **Methadone:** RPV mildly reduces methadone concentrations.	• **Methadone:** Monitor for signs of methadone withdrawal; increase dose as necessary. • **Methadone, BUP:** Use cautiously with RPV; supratherapeutic doses of RPV have been known to cause increase in QT prolongation.
Efavirenz (EFV)	• **BUP:** When given with BUP (monotherapy), EFV significantly reduces BUP concentrations, but no patients developed opioid withdrawal. • **Methadone:** EFV induces methadone metabolism via CYP3A4 and reduces methadone concentrations.	• **BUP:** When given with BUP, dose adjustments are unlikely to be required, but monitor for withdrawal symptoms. If withdrawal symptoms occur, increase BUP dose accordingly. • **Methadone:** Titrate to achieve clinical effect; monitor for signs and symptoms of opioid withdrawal.

Table 43: Methadone, Buprenorphine (BUP), Naloxone (NLX), and Naltrexone [a] (also see prescribing information)		
Class or Drug	**Mechanism of Action**	**Clinical Comments**
Etravirine (ETR)	• **BUP:** No significant interactions are expected. • **Methadone:** ETR may slightly increase methadone concentrations.	• **BUP, methadone:** Titrate opioid or antagonist as required to achieve clinical effect; monitor for signs of withdrawal or opioid toxicity. • **Methadone:** Monitor for signs of methadone toxicity and reduce dose if necessary.
Lenacapavir (LEN)	**Methadone, BUP:** Moderate inhibition of CYP3A4 and P-gP potentially increases methadone or BUP levels.	• **Patients initiating MAT while already on LEN:** Initiate MAT at lowest initial or maintenance dose. • **Patients initiating LEN while already on MAT:** MAT dose adjustments may be needed. • Monitor for excess sedation and/or respiratory depression.
Abbreviations: ARV, antiretroviral; CYP, cytochrome P450; MAT, medication-assisted therapy; NRTI, nucleoside reverse transcriptase inhibitor; P-gP, P-glycoprotein; PI, protease inhibitor. **Note:** a. No significant interactions are expected between ARVs, naloxone, and naltrexone.		