

## APPENDIX XI

### INTERACTIONS BETWEEN HIV-RELATED MEDICATIONS AND MEDICATIONS USED IN THE TREATMENT OF OPIOID (HEROIN AND PRESCRIPTION OPIOID) ADDICTION

<b>TABLE 1</b>				
<b>INTERACTIONS BETWEEN HIV-RELATED MEDICATIONS AND MEDICATIONS USED IN THE TREATMENT OF OPIOID (HEROIN AND PRESCRIPTION OPIOID) ADDICTION</b>				
	<b>Methadone</b>		<b>Buprenorphine</b>	
<b>Medication</b>	<b>Effect on Methadone</b>	<b>Effect on Medication</b>	<b>Effect on Buprenorphine</b>	<b>Effect on Medication</b>
<b>NRTI</b>				
<b>Abacavir (ABC)</b>	↑ Methadone clearance, but dose adjustment not needed	↑ Time to peak concentration, ↓ Peak concentration	Unknown, but interaction unlikely	Unknown, but interaction unlikely
<b>Didanosine (ddI)</b>	None reported	↓ ddi AUC by 57% (with buffered formulation). Use ddi EC with methadone co-administration.	Unknown, but interaction unlikely	Unknown, but interaction unlikely
<b>Emtricitabine (FTC)</b>	Not studied, but interaction unlikely	Not studied, but interaction unlikely	Unknown, but interaction unlikely	Unknown, but interaction unlikely
<b>Lamivudine (3TC)</b>	None	None	Unknown, but interaction unlikely	Unknown, but interaction unlikely
<b>Stavudine (d4T)</b>	None	↓ d4T AUC by 27%. Unlikely to be significant; use standard dose.	Unknown, but interaction unlikely	Unknown, but interaction unlikely
<b>Tenofovir (TDF)</b>	None reported	None	Unknown, but interaction unlikely	Unknown, but interaction unlikely
<b>Zidovudine (AZT)</b>	None	↑ ZDV AUC by 43%. Monitor for ZDV adverse reactions.	Unknown, but interaction unlikely	No change in ZDV AUC

<b>NNRTI</b>				
<b>Delavirdine (DLV)</b>	Not evaluated. May ↑ methadone; monitor with co-administration	Not affected	Potential ↑ buprenorphine activity	No data, but change in DLV not expected
<b>Efavirenz (EFV)</b>	↓ Methadone levels by 52%; may need to ↑ methadone dose to prevent heroin relapse	Not reported, but unlikely to affect EFV	↓ Buprenorphine AUC 50%, but no withdrawal symptoms observed	Not affected
<b>Etravirine (ETR)</b>	No change in active R-methadone; no dose modification likely, but monitor for withdrawal symptoms	ETR PK parameters comparable to historical control	No data. May ↓ buprenorphine serum concentration.	No data; ETR unlikely to be affected
<b>Nevirapine (NVP)</b>	↓ Methadone levels by 46%; may need to ↑ methadone dose to prevent heroin relapse	Not studied or reported	Potential ↓ buprenorphine activity	No data, but change in NVP not expected
<b>PI</b>				
<b>Amprenavir (APV)</b>	↓ Active methadone levels by 13%, but no withdrawal symptoms observed	↓ APV 25%	Potential ↑ buprenorphine activity	No data, but change in APV not expected
<b>Atazanavir (ATV)</b>	Not affected with unboosted ATV. Monitor for withdrawal with ATV/r.	Not measured	With ATV and ATV/r co-administration, buprenorphine AUC ↑ 92% and 67%. Some patients experienced ↑ sedation.	Not affected

<b>Darunavir (DRV)</b>	↓ AUC <sub>24h</sub> 16%, symptoms associated with opiate withdrawal observed in some patients. May need to ↑ dose.	None	Potential ↑ buprenorphine activity	No data, but change in DRV not expected
<b>Fosamprenavir (FPV)</b>	↓ Methadone AUC 18%, but no significant change in the unbound R-methadone. No withdrawal symptoms observed.	Not measured	Potential ↑ buprenorphine activity	No data, but change in FPV not expected
<b>Indinavir (IDV)</b>	No change	No change	Potential ↑ buprenorphine activity	No data, but change in IDV not expected
<b>Lopinavir/ ritonavir (LPV/r)</b>	↓ Methadone AUC 26-36%. Conflicting data on withdrawal symptoms – monitor for need to ↑ methadone dose	Not reported	No significant change	No significant change
<b>Nelfinavir (NFV)</b>	No change in R-methadone; no withdrawal symptoms observed	None	No significant change	No significant change
<b>Ritonavir (RTV)</b>	↓ Methadone AUC 36% (studied with high-dose RTV). Monitor for withdrawal symptoms with low-dose boosted RTV co-administration.	None reported	Potential ↑ buprenorphine activity	No data, but change in RTV not expected

<b>Saquinavir (SQV)</b>	↓ Methadone R-isomer AUC 20% (studied with RTV/SQV 400/400 mg bid); monitor for need to ↑ methadone dose	None reported	Potential ↑ buprenorphine activity	No data, but change in SQV not expected
<b>Tipranavir (TPV)</b>	↓ Methadone AUC 50%; may require ↑ in methadone dose	None	Buprenorphine AUC not affected, but ↓ norbuprenorphine (active metabolite) AUC ~80%. No withdrawal symptoms observed.	Compared to historical control, TPV AUC ↓ 26%; monitor for antiviral efficacy
<b>FI</b>				
<b>Enfuvirtide (T-20)</b>	Not studied; interaction unlikely	Not studied	No data; interaction unlikely	No data; interaction unlikely
<b>CCR5 Co-receptor Antagonist</b>				
<b>Maraviroc (MVC)</b>	Not studied; interaction unlikely	Not studied; interaction unlikely	No data; interaction unlikely	No data; interaction unlikely
<b>Integrase Inhibitor</b>				
<b>Raltegravir (RAL)</b>	Not studied; interaction unlikely	Not studied; interaction unlikely	No data; interaction unlikely	No data; interaction unlikely
<b>Other common medications used in the treatment of HIV-infected persons</b>				
<b>Carbamazepine</b>	↓ Methadone levels; consider using valproic acid or levetiracetam as an alternative	None reported	May ↓ buprenorphine activity	No data but change of carbamazepine unlikely
<b>Fluconazole</b>	↑ Methadone levels by ~30%; monitor for symptoms of opioid toxicity	None reported	May ↑ buprenorphine activity	No data but change of fluconazole unlikely

<b>Phenobarbital</b>	↓ Methadone levels, often sharply; consider using valproic acid or levetiracetam as an alternative	None reported	May ↓ buprenorphine activity	No data but change of phenobarbital unlikely
<b>Phenytoin</b>	↓ Methadone levels, often sharply; consider using valproic acid or levetiracetam as an alternative	None reported	May ↓ buprenorphine activity	No data but change of phenytoin unlikely
<b>Rifabutin</b>	No effect on methadone	None reported	May ↓ buprenorphine activity	No data but change of rifabutin unlikely
<b>Rifampin</b>	↓ Methadone levels 33-68%; ↑ methadone dose	None reported	May ↓ buprenorphine activity	No data but change of rifampin unlikely