



# Opioid Drug-Drug Interactions

[www.sempguidelines.org](http://www.sempguidelines.org)



West Virginia  
Safe & Effective Management of Pain  
(SEMP) Guidelines

Opioid	CYP450 Enzyme	Common Interacting Medications(s)	Result	Comments
codeine	2D6	celecoxib, duloxetine, bupropion, fluoxetine, & paroxetine	Inhibit conversion to active metabolite	Decreased Analgesia
	n/a	SSRIs/SNRIs	Increased central serotonin levels	Monitor for Serotonin Syndrome
fentanyl	3A4	clarithromycin, diltiazem, verapamil, & erythromycin	Increased fentanyl concentration	Adjust fentanyl dose
meperidine	n/a	acyclovir	Increased meperidine concentration	n/a
	3A4	phenytoin, carbamazepine, & phenobarbital	Decreased meperidine concentration	n/a
	n/a	SSRIs/SNRIs	Increased central serotonin levels	Monitor for Serotonin Syndrome
	n/a	cimetidine	Increased meperidine concentration	Choose alternative H2RA
morphine	n/a	rifampin & ranitidine	Decreased morphine concentration & conversion to active metabolite	May result in decreased analgesia
methadone	2D6	celecoxib, duloxetine, bupropion, fluoxetine, & paroxetine	Increased methadone concentration	Reduce dose of methadone
	3A4	phenytoin, carbamazepine, & phenobarbital	Decreased methadone concentration	May precipitate opioid withdrawal
	3A4	clarithromycin, diltiazem, verapamil, & erythromycin	Increased methadone concentration	Reduce dose of methadone
tramadol	2C9	carbamazepine	Increases tramadol metabolism	Avoid combination
	2D6	celecoxib, duloxetine, bupropion, fluoxetine, & paroxetine	Inhibit conversion to active metabolite	Decreased Analgesia
	n/a	SSRIs/SNRIs	Increased central serotonin levels	Monitor for Serotonin Syndrome
hydrocodone	2D6	celecoxib, duloxetine, bupropion, fluoxetine, & paroxetine	Inhibit conversion to active metabolite	Decreased Analgesia
	3A4	clarithromycin, diltiazem, verapamil, & erythromycin	Increased hydrocodone levels	Adjust hydrocodone dose
oxycodone	2D6	celecoxib, duloxetine, bupropion, fluoxetine, & paroxetine	Increased oxycodone levels, but decreased oxymorphone (metabolite) levels	n/a
	3A4	phenytoin, carbamazepine, & phenobarbital	Decreased oxycodone concentration	Decreased Analgesia
	3A4	clarithromycin, diltiazem, verapamil, & erythromycin	Increased oxycodone levels	Adjust oxycodone dose

1. Clinical Pharmacology [Internet database]. Gold Standard, Inc., 2007. Available at: <http://www.clinicalpharmacology.com>. Accessed June 2016.
2. Common Opioid-Drug Interactions: What Clinicians Need to Know. Practical Pain Management, 2012.