

Buprenorphine/naloxone Drug–Drug Interactions

Common drug–drug interaction		Comment	Action
Category	Examples		
CNS depressants	Anti-depressants Anti-emetics Anti-histamines Anti-psychotics Anxiolytics Muscle relaxants Neuroleptics Other opioids Phenothiazines Sedatives/hypnotics Tranquilizers	The additive depressant effect increases the risk of respiratory depression, profound sedation, coma, and death.	Use caution when co-prescribing OAT and CNS depressants. Dosage and duration should be limited to the minimum required. Closely monitor patients on these combinations for signs of sedation and respiratory depression. Benzodiazepines should only be co-prescribed with OAT as part of a benzodiazepine taper. Consult prior to prescribing OAT if uncertain.
Alcohol	Medications containing alcohol	The additive depressant effect increases the risk of respiratory depression, profound sedation, coma, and death.	Medications containing alcohol are contraindicated and, if needed, should be assessed and co-administered with caution.
Opioid antagonists and mixed agonist/antagonist	Naltrexone	Contraindicated. Blocks the pharmacological effects of buprenorphine, which can lead to precipitated withdrawal.	Avoid co-prescribing opioid antagonists with OAT. Patient may require a different medication (e.g., acamprosate for alcohol use disorder).
CYP3A4 inhibitors	Azole antifungals Macrolide antibiotics Protease inhibitors	May require buprenorphine/naloxone dose reduction or a change in antibiotic or antifungal.	Closely monitor patient. Consult prior pharmacy or other resources to prescribing if uncertain.
CYP3A4 inducers	Carbamazepine Phenobarbital Phenytoin Rifampicin	May result in under treatment of opioid use disorder. May require dose adjustment of CYP3A4 inducer or buprenorphine/naloxone.	Closely monitor patient. Consult pharmacy or other resources prior to prescribing if uncertain.
Serotonergic medications	SSRIs Citalopram Escitalopram Fluoxetine Fluvoxamine Paroxetine Sertraline Vilazodone SNRIs Desvenlafaxine Duloxetine Levomilnacipran Milnacipran Venlafaxine MAOIs Isocarboxazid Phenelzine Tranylcypromine	Theoretical increase in the risk of serotonin syndrome.	Monitor patient and consult if uncertain.

Abbreviations: CYP3A4: cytochrome P450 3A4; MAOI: monoamine oxidase inhibitor; OAT: opioid agonist treatment; SNRI: serotonin-norepinephrine reuptake inhibitor; SSRI: selective serotonin reuptake inhibitor.

Note on cytochrome P450 3A4

- Buprenorphine is metabolized by the cytochrome P450 3A4 (CYP3A4) enzyme system.
 - Drugs that are known to inhibit or induce CYP3A4 have the potential to diminish or enhance buprenorphine metabolism.
 - However, these interactions are clinically less relevant than those with methadone—it is rare the buprenorphine dose needs to be adjusted.