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Alcohol and Drug Interactions

Many drugs interact with alcohol to some extent. There are two main types of alcohol-drug interactions: pharmacokinetic and pharmacodynamic. Pharmacokinetic interactions occur when alcohol alters the metabolism or excretion of the drug or vice versa. Pharmacodynamic interactions refer to additive effects of alcohol and certain drugs, particularly in the central nervous system (e.g., sedation).[1] Alcohol is primarily metabolized in the liver by several enzymes. The most important enzymes are aldehyde dehydrogenase and CYP2E1. In people consuming alcohol occasionally, CYP2E1 metabolizes only a small fraction of the ingested alcohol. In contrast, chronic heavy drinking can increase CYP2E1 activity up to ten-fold, resulting in higher proportion of alcohol being metabolized by CYP2E1 rather than alcohol dehydrogenase. Therefore, the effect of alcohol on the interacting drug may be different depending on chronic or acute alcohol use.[3] Alcohol can also increase the risk of hepatoxicity with some drugs. See our *PL Chart, Liver Function Test Scheduling*, for more on drugs that require liver function monitoring. **Alcohol is contraindicated with a number of extended-release formulations (e.g., *Opana ER* [U.S.], various other opioids) due to the risk of dose dumping of the formulation or increased availability of the drug and potential overdose**.[2] Many other extended-release formulations also have warnings about alcohol such as *Ritalin LA* (U.S.), *Gralise* (U.S.), *Durlaza* (U.S.), etc.[4,15,26] In general, be cognizant of patients who are using extended-release formulations and counsel on the potential risks associated with alcohol consumption. In addition, remind patients that some OTC meds (e.g., cough syrups, laxatives) may contain up to 10% alcohol.[8] Finally, it is important to note that the elderly may be at higher risk with alcohol-drug interactions, due to the fact that alcohol metabolism may be slowed and alcohol itself may increase the risk of falls, serious injury, etc.[8] This chart includes selected alcohol-drug interactions and recommendations for alcohol consumption. Note that the chart is not all-inclusive and that product labeling for meds may advise avoiding use with alcohol due to the potential for additive CNS effects. In addition, **comorbidities related to alcoholism such as cirrhosis, GI effects, etc, may require additional considerations related to drug therapy**.

Abbreviations: CNS=central nervous system; GI=gastrointestinal; MAOIs=monoamine oxidase inhibitors; NSAIDs= nonsteroidal anti-inflammatory drugs; PDE-5=phosphodiesterase-5; TCAs=tricyclic antidepressants.

Drug or Drug Class	Clinical Effects and Possible Mechanisms	Recommendations and Comments
Analgesics (Non-Opioids)		
Acetaminophen	• Chronic alcohol use can increase blood levels of the acetaminophen metabolite, N-acetyl-p-benzoquinoneimine (NAPQ), which is hepatotoxic, and reduce blood levels of acetaminophen. The mechanism is increased metabolism of acetaminophen by CYP2E1.[1,5] It may also increase the risk of kidney disease through an unknown mechanism.[6] • Acute alcohol use in large amounts may increase the risk of liver toxicity with acetaminophen similar to chronic alcohol use[5]	• U.S. product labeling for acetaminophen products states that severe liver damage may occur in adults who have ≥3 alcoholic drinks/day while taking acetaminophen[7]

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Drug or Drug Class	Clinical Effects and Possible Mechanisms	Recommendations and Comments
Analgesics (Non-Opioids), continued		
Aspirin NSAIDs	• Aspirin or NSAIDs and alcohol may have additive or synergistic damaging effects on the gastric mucosal barrier leading to an increased risk of GI hemorrhage, in a dose-dependent manner[1,5,7,8]	• Advise against chronic NSAID use in regular drinkers, especially in heavy drinkers (e.g., ≥3 alcoholic drinks/day)[9] • Product labeling for aspirin extended-release capsules (*Durlaza*) recommend not taking the drug within 2 hours prior or 1 hour following consumption of alcohol due to possible interference of alcohol with the controlled-release property of the formulation[26]
Analgesics (Opioids): ***In addition to enhanced sedative effects, concurrent use of alcohol and opioids increases the risk of fatal overdose due to respiratory depression***.[1,8,10]		
Extended-release opioids	• Co-ingestion of alcohol and some extended-release opioids may lead to "dose dumping" or delivery of a potentially fatal dose of the opioid[7]	• In general, advise against concomitant use of alcohol and all opioids[22] • Extended-release formulations that are known to be adversely affected by alcohol include *Nucynta ER*, *Opana ER* (U.S.), *Embeda* (U.S.), *Kadian*, and *Zohydro ER* (U.S.)[2,27-30,35,36]
Methadone	• Chronic alcohol use reduces the effects of methadone due to increased hepatic metabolism of methadone[7] • Acute alcohol ingestion increases the effects of methadone due to decreased hepatic metabolism of methadone[7]	• Warn patients about the potential effects of alcohol on methadone, such as an increased risk of fatal overdose. In general, advise against concomitant use of alcohol and opioids.[7,22]
Anticoagulants/Antiplatelets: ***Alcohol may increase the risk of falls, and therefore the risk of bleeding, with anticoagulants/antiplatelets.***[12]		
Warfarin	• Acute ingestion of alcohol may reduce metabolism of warfarin,[10] although small to moderate amounts (2 to 3 drinks) don't seem to have an effect[11] • Chronic use of alcohol has been associated with both increases and decreases in the effects of warfarin and there are conflicting data.[5,10,11] Patients with liver disease may be more likely to have potentiation of warfarin's effects with alcohol use.[12]	• Advise patients about the potential effects of alcohol use on the effects of warfarin, and monitor more frequently if dietary habits, including alcohol consumption, change[12]

Drug or Drug Class	Clinical Effects and Possible Mechanisms	Recommendations and Comments
Antidepressants		
Bupropion	• Bupropion may reduce alcohol tolerance[7,10] • Both acute alcohol ingestion and abrupt discontinuation of alcohol use can increase the risk for seizures, and bupropion can also reduce the seizure threshold[10]	• Advise patients to minimize or avoid the use of alcohol with bupropion[10]
MAOIs	• Tyramine, which is found in some beers and wines, interacts with MAOI inhibitors leading to severe hypertension.[10,13] • Alcohol and MAOIs may have additive CNS effects[10]	• Advise patients to avoid the use of alcohol with MAOIs[1] • In general, dietary restrictions for MAOIs should be followed for at least two weeks following discontinuation of MAOIs[10]
TCAs	• Alcohol may increase the sedative effects of tricyclic antidepressants, their blood levels (e.g., amitriptyline), and the risk of orthostatic hypotension.[1,3,5,7,12,13]	• Consider the use of SNRIs or SSRIs for patients who consume alcohol, as the risk for an interaction appears to be limited[1] • Alcohol-enhanced CNS depression may be more prevalent in the first week of TCA therapy[7]
Antidiabetics: ***Alcohol suppresses gluconeogenesis and may generally increase the risk of hypoglycemia.***[1] ***However, there may also be a risk that calories from alcohol consumption can worsen glycemic control.***[10,14]		
Sulfonylureas	• Alcohol may cause a disulfiram-like reaction in patients who are taking chlorpropamide, glyburide, tolazamide, or tolbutamide[1,8]	• Advise patients taking sulfonylureas against heavy alcohol consumption and to avoid alcohol completely during the fasting state or if symptoms of hypoglycemia occur after any consumption[14]
Insulins	• Alcohol ingestion may cause severe and unpredictable effects of insulin on blood sugar due to its effects on gluconeogenesis[14]	• Advise patients using insulin against heavy alcohol consumption and to avoid consumption of alcohol on an empty stomach[14]
Metformin	• Concomitant ingestion of alcohol and metformin may cause nausea and weakness[8] • Alcohol ingestion may lead to increased blood levels of lactic acid with metformin use[1,25]	• Advise patients taking metformin against heavy alcohol consumption, either acute or chronic, and to monitor for signs and symptoms of lactic acidosis (e.g., muscle or stomach pain, slowed heart rate, dizziness) if alcohol is consumed[25]

Drug or Drug Class	Clinical Effects and Possible Mechanisms	Recommendations and Comments
Antiepileptics: ***Moderate social drinking does not seem to cause a clinically relevant interaction in most cases, although additive sedation can be an issue.***[7,10]		
Perampanel *Fycompa*	• Concomitant use of alcohol and perampanel (especially high doses) can lead to an increased risk of CNS depression and psychiatric effects such as anger, confusion, and depression[10]	• Advise patients about possible effects of alcohol and perampanel, and recommend limiting activity until the effects of concomitant use are known for each individual.[10] (Avoid use of alcohol per Canadian labeling.)[31]
Phenytoin	• Acute alcoholic intake may increase phenytoin levels, while chronic alcohol use may decrease levels[33]	• Advise patients about possible effects of alcohol and phenytoin
Antihistamines: ***Drowsiness may be increased when antihistamines are used with alcohol, and psychomotor effects such as on driving abilities may be significantly impacted, especially with sedating antihistamines.***[7]		
First-generation antihistamines	• Alcohol may increase sedation and dizziness associated with first-generation antihistamines, especially in older adults, due to additive CNS effects[1,8,13]	• Advise against alcohol consumption with first-generation antihistamines.[22] Consider recommending a non-sedating antihistamine instead of a first-generation antihistamine, but warn patients about the possibility of an interaction since responses may differ between individuals.[7]
Antihypertensives: ***Moderate to heavy chronic drinking (>2 drinks/day) increases blood pressure.***[7,16] ***In addition, alcohol consumption can acutely lead to hypotension and additive effects with vasodilators.***		
Alpha-1-adrenergic blockers	• Alcohol may increase the risk of postural hypotension with alpha-blockers, shortly after its ingestion[8]	• Advise patients about possible effects of alcohol and alpha-blockers
Beta-blockers	• Alcohol may increase the hypotensive effects of beta-blockers[7]	• Advise patients about possible effects of alcohol and beta-blockers
Calcium channel blockers	• Alcohol may increase the risk of postural hypotension with calcium channel blockers, shortly after its consumption[5,7] • Chronic use of verapamil may increase blood levels of alcohol and reduce its rate of metabolism[7] • Alcohol may increase blood levels of nifedipine[5]	• Advise patients about possible effects of alcohol and calcium channel blockers

Drug or Drug Class	Clinical Effects and Possible Mechanisms	Recommendations and Comments
Antimicrobials		
Doxycycline	• Chronic heavy use of alcohol may lead to subtherapeutic levels of doxycycline due to an increase in its rate of metabolism[7]	• Consider doubling the dose of doxycycline in alcoholic patients or substitute a non-interacting drug for doxycycline[7] • Note that concurrent ingestion of ethanol and tetracycline may slightly increase blood levels of tetracycline[10]
Griseofulvin (U.S.)	• Griseofulvin may increase the effects of alcohol, such as nausea, vomiting, tachycardia, and severe hypotension[8,17,22]	• Advise patients to avoid alcohol while taking griseofulvin[22]
Isoniazid	• Heavy or chronic alcohol ingestion (i.e., daily) may increase the risk of hepatotoxicity with isoniazid and increase the clearance of isoniazid[7,8,10,22]	• Advise patients to avoid alcohol while taking isoniazid[10,22,24]
Ketoconazole	• Alcohol may increase the risk of a disulfiram-like reaction with oral ketoconazole[7] • Alcohol may increase the risk of hepatotoxicity with oral ketoconazole[24]	• Advise patients to avoid alcohol while taking ketoconazole[7]
Metronidazole	• Alcohol may increase the risk of a disulfiram-like reaction with metronidazole. There may also be a risk with vaginal metronidazole formulations due to small amounts of systemic absorption, although it appears to be small.[7]	• The risk may be low, but advise patients to avoid alcohol while taking metronidazole and for 72 hours after metronidazole has been stopped[7,22]
Tinidazole (U.S.)	• Alcohol may increase the risk of a disulfiram-like reaction with tinidazole[7]	• The risk may be low, but advise patients to avoid alcohol while taking tinidazole and for 72 hours after it has been stopped[7,22]
Antipsychotics		
Atypicals	• Concomitant use of alcohol and atypical antipsychotics can lead to additive CNS effects and postural hypotension, especially with olanzapine and quetiapine[7]	• Advise patients to avoid alcohol while taking antipsychotics[7,22]
Phenothiazines	• Concomitant use of alcohol and phenothiazines can lead to an increased risk of sedation[13] • May increase the risk of extrapyramidal side effects[7]	• Advise patients to avoid alcohol while taking antipsychotics[22]

Drug or Drug Class	Clinical Effects and Possible Mechanisms	Recommendations and Comments
Muscle Relaxants: ***Concurrent use of muscle relaxants and even small amounts of alcohol can lead to additive CNS depressant effects.***[7]		
Sedative-Hypnotics		
Barbiturates	• Concomitant use of barbiturates and even small amounts of alcohol can lead to additive CNS effects[7]	• Warn patients of possible effects, such as increased sedation and impaired psychomotor skills, as well as the potential for hangover effects where a barbiturate could continue to interact with alcohol the next day[7]
Benzodiazepines	• Concomitant use of benzodiazepines and alcohol can lead to additive CNS effects. This is especially true with long-acting benzodiazepines or with greater amounts of alcohol[7,10] • Acute alcohol ingestion may increase blood levels of some benzodiazepines (e.g., diazepam, triazolam) by increasing their absorption[7,10]	• Warn patients of possible effects, such as increased sedation and impaired psychomotor skills.[7] Consider advising against concomitant use of alcohol and benzodiazepines.[22]
Non-benzodiazepine hypnotics (e.g., "Z drugs," ramelteon, suvorexant [*Belsomra*])	• Concomitant use of alcohol and non-benzodiazepine hypnotics can lead to additive CNS effects and risk of "complex behaviors" (e.g., sleep-driving, etc)[5,23]	• Advise against the use of alcohol with non-benzodiazepine hypnotics.[22] Besides interacting with these drugs, alcohol is associated with insomnia.[18]
Chloral hydrate	• Concomitant use of alcohol and chloral hydrate can lead to additive CNS effects in addition to reduced metabolism of both agents[10]	• Advise patients to separate consumption of significant amounts of alcohol from the use of chloral hydrate by 12 to 24 hours[10]
Meprobamate (U.S.)	• Meprobamate can increase alcohol-associated intoxication[7] • Chronic use of alcohol may increase metabolism of meprobamate[8]	• Advise patients to avoid alcohol while taking meprobamate[7]
Sexual Dysfunction Treatments		
Flibanserin (U.S.) (*Addyi*)	• Concomitant use of alcohol and flibanserin may lead to severe hypotension and syncope[19]	• Advise patients to abstain from alcohol (from any source) during treatment with flibanserin and for 2 days after discontinuation.[19]
PDE5 inhibitors (e.g., sildenafil, etc)	• Concomitant use of alcohol and PDE-5 inhibitors may rarely increase the risk of postural hypotension and increased heart rate (seen with tadalafil), especially when several drinks are consumed[7]	• Advise patients about the possible effects of alcohol and PDE-5 inhibitors, and remind them that alcohol can worsen erection difficulties as well[7]

Drug or Drug Class	Clinical Effects and Possible Mechanisms	Recommendations and Comments
Statins: ***Alcohol abuse may increase the risk of side effects with statins***.[34]		
Miscellaneous Agents		
Acitretin	• Increased duration of teratogenic potential in women[10] • Alcohol increases the transesterification of acitretin to etretinate, a teratogen which can remain in the body for years[10]	• Tell women of reproductive potential to completely avoid alcohol and alcohol-containing drugs while taking acitretin and for 2 months after the drug is stopped[10]
Methotrexate	• Ingestion of ~2 or more alcoholic drinks per week may increase the risk of methotrexate-induced liver toxicity.[7] Patients being treated for psoriasis may be at higher risk than those being treated for rheumatoid arthritis.[20]	• Consider advising patients against consumption of alcohol during treatment with methotrexate.[7] See our *PL Detail-Document, Using Methotrexate Safely for Rheumatoid Arthritis*, for more information.
Metoclopramide	• Concomitant use of alcohol and metoclopramide can lead to additive CNS effects[7] • Metoclopramide may increase blood levels of alcohol due to increased gastric emptying[7]	• Consider advising patients to avoid alcohol while taking metoclopramide[21]
Varenicline *Champix*-Canada, *Chantix*-U.S.	• Concomitant use of alcohol may increase alcohol-associated intoxication, and increase the risk of unusual or aggressive behavior[10] (per Canadian labeling, increased risk of psychiatric adverse events).[32]	• Advise patients about possible effects of alcohol and varenicline, and recommend limiting alcohol intake until the effects of concomitant use are known for each individual[10,32]

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