Alcohol Use Disorder

Effective medications exist and almost nobody gets one · undertreatment is the defining failure, not a shortage of options

Offer a medication
reduction counts as success

⚠ THE TWO BELIEFS DOING THE DAMAGE

⚠ "NALTREXONE IS UNSAFE IN LIVER DISEASE"

Wrong, and it withholds treatment from exactly the patients whose survival depends on stopping. The **FDA boxed warning was removed in 2013** -the evidence did not support it, and it came from doses far above those used for AUD. **Studies including patients with cirrhosis have not shown meaningful drug-induced liver injury**, and current guidance treats it as usable in compensated and even decompensated disease. **DISULFIRAM, not naltrexone, is the agent genuinely contraindicated in significant liver disease.**

⚠ "WAIT UNTIL THEY COMMIT TO ABSTINENCE"

Demanding abstinence up front loses the patients who would have accepted treatment. Reduced drinking is a real clinical outcome -moving down a drinking-risk level lowers harm- and **naltrexone is specifically best evidenced for reducing HEAVY DRINKING rather than producing total abstinence.** It can be started **while the patient is still drinking.** Ask what they want to change and treat toward that.

SCREEN EVERYONE

Single-item screener: how many times in the past year have you had **5+ drinks in a day (men) / 4+ (women)**? **Any answer above zero is positive.** Or **AUDIT-C** (3 items, 0-12). Screening by stereotype is how **the professional, the older patient and the woman get missed. DSM-5: 2-3 mild, 4-5 moderate, 6+ severe** -severity sets urgency, not eligibility.

THE MEDICATIONS *naltrexone and acamprosate are first-line; the rest are second-line*

Drug	Mechanism & role	Practical points
Naltrexone FIRST-LINE	**Opioid antagonist**; blunts the rewarding effect of drinking Best for REDUCING heavy drinking	**50 mg PO daily** (both the starting and target dose), or a **monthly extended-release intramuscular injection every 28 days** when adherence is the obstacle -often the deciding practical advantage. **Start without requiring abstinence.** ⚠ **Absolutely incompatible with opioids:** precipitates withdrawal in anyone opioid-dependent and **blocks opioid analgesia**, so avoid with concurrent opioid use or anticipated opioid pain control
Acamprosate FIRST-LINE	**Modulates glutamatergic signaling**, stabilizing the post-alcohol hyperexcitable state MAINTAINS abstinence	**666 mg PO three times daily** (two 333 mg tablets per dose). **Works best in someone who has already stopped**, so it suits the post-withdrawal patient. **Renally cleared** -dose-reduce in impairment, avoid in severe impairment, check renal function first. **Three-times-daily dosing is its main weakness** and a common reason it fails in practice
Topiramate off-label	Glutamate antagonism + GABA facilitation	**Off-label but well supported** -reduces heavy drinking and improves abstinence, with evidence suggesting an effect at least comparable to the approved agents. **Titrate slowly**: cognitive slowing, word-finding difficulty, paresthesias, weight loss, small stone risk. A reasonable next step after a first-line failure
Gabapentin off-label	Calcium channel subunit modulation	**Useful when protracted withdrawal, insomnia or anxiety dominate**, treating those alongside the drinking. Renally cleared. Misuse potential, especially with concurrent opioid use, so not a default
Disulfiram not first-line	**Inhibits aldehyde dehydrogenase** → acetaldehyde accumulates, drinking becomes aversive	**A deterrent, NOT anti-craving** -it does nothing for the desire to drink, so it works only in a highly motivated patient and **evidence is strongest with SUPERVISED administration.** Reaction (flushing, vomiting, hypotension) can be severe. ⚠ **Contraindicated in significant liver disease**, avoid in cardiovascular disease, and beware the reaction with **metronidazole** and hidden alcohol in other preparations

CHOOSING BETWEEN THEM

Clinical situation	Preferred agent, and why
Still drinking, wants to cut down	**Naltrexone** -no abstinence required to start, best evidence for reducing heavy drinking
Already abstinent, staying that way	**Acamprosate** -its evidence is for maintaining abstinence in someone already stopped
Significant renal impairment	**Naltrexone** -acamprosate is renally cleared
Advanced decompensated liver disease	**Acamprosate** is reasonable, but **naltrexone is not the contraindication it was believed to be. Avoid disulfiram**
⚠ Concurrent opioid use / opioid analgesia	**NOT naltrexone** -precipitates withdrawal and blocks pain control. Use acamprosate, or consider topiramate or gabapentin
Adherence is the obstacle	**Extended-release injectable naltrexone** removes the daily decision; or supervised disulfiram with a reliable observer
First-line agent failed	**Topiramate**, or switch between first-line agents. **Failure of one medication is not failure of pharmacotherapy** -sequential trials are normal in a relapsing disease

WHAT ELSE TO GET RIGHT

QUANTIFY PROPERLY

One US standard drink = ~14 g alcohol = 12 oz beer (~5%), 5 oz wine (~12%), 1.5 oz spirits (~40%). Patients under-report because a home pour or craft beer is often two standard drinks, so count in these units rather than accepting "a couple of glasses." **At-risk: >4/day or >14/week (men), >3/day or >7/week (women)** -lower in women from differences in body water and first-pass metabolism.

READ THE LIVER PROPERLY

AST:ALT > 2 with both only modestly raised suggests alcohol-associated injury, versus the ALT-predominant pattern of MASLD. **Thrombocytopenia is an early, often-dismissed clue to advanced fibrosis. Normal enzymes do NOT exclude significant drinking**, and most alcohol-associated liver disease is silent until advanced -so assess fibrosis non-invasively rather than waiting for decompensation.

⚠ DO NOT FORGET

Thiamine before or with glucose -a glucose load can precipitate **Wernicke encephalopathy**, a clinical diagnosis often missed because the triad is usually incomplete. Replace **magnesium, potassium, phosphate**; watch refeeding. **Ask about prior withdrawal seizures or DTs**: they predict complicated withdrawal, and **abrupt unsupervised cessation is genuinely dangerous** in those patients.

PEARLS & PITFALLS

- **Treating the withdrawal and arranging nothing is the commonest error** -it is the same omission as an opioid detox with no medication to follow. **Withdrawal severity escalates with repeated untreated episodes.**
- **Medication and behavioral treatment each help, and neither is a prerequisite for the other.** Withholding the prescription until the patient enters counseling mostly succeeds in delaying treatment.
- **Plan for relapse rather than treating it as failure.** A patient who returns after a lapse has done the right thing; responding with disappointment teaches them not to come back.
- **Treat comorbid depression and anxiety concurrently, not sequentially** -waiting for sobriety leaves the untreated condition driving relapse.

References: VA/DoD clinical practice guideline for the management of substance use disorders (naltrexone and acamprosate first-line; disulfiram, topiramate and gabapentin second-line) · FDA removal of the naltrexone hepatotoxicity boxed warning (2013) and subsequent cirrhosis safety data · NIAAA definitions of a standard drink and at-risk drinking · DSM-5 criteria for alcohol use disorder.

Educational aid; verify against current guidance, local formulary and patient factors.

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