SUBSTANCE USE DISORDER AGENT

Acamprosate

Campral (brand discontinued in the US; generics available)

Glutamate-modulating anti-relapse agent for alcohol use disorder in patients already abstinent, safe in liver disease and with opioids.

USUAL ADULT DOSE	HALF-LIFE	METABOLISM	ONSET
666 mg PO TID with meals	20-33 h	None; renal excretion unchanged	Steady state in 5-7 days

No FDA boxed warning on the current US label.

INDICATIONS

- FDA-approved for maintenance of abstinence from alcohol in adults with alcohol dependence who are already abstinent, alongside psychosocial treatment.
- Listed with naltrexone as first-line pharmacotherapy for alcohol use disorder by the APA 2018 guideline and the VA/DoD 2021 guideline.
- Best matched to patients whose stated goal is complete abstinence, whereas naltrexone chiefly reduces heavy drinking days.
- Preferred when hepatic disease, ongoing opioid analgesia or opioid agonist therapy makes naltrexone unsuitable or contraindicated.
- Not effective for managing acute alcohol withdrawal and has no role in detoxification; benzodiazepines or phenobarbital cover that phase.
- Off-label trials in gambling disorder, anxiety, tinnitus and fragile X syndrome exist but the evidence is too thin to support routine use.

DOSING & TITRATION

- Standard adult dose is two **333 mg** delayed-release tablets (**666 mg**) three times daily with meals, begun as soon as abstinence is achieved.
- Start after withdrawal is complete, ideally within days of the last drink; delaying initiation reduces the chance of sustained abstinence.
- Reduce to one **333 mg** tablet three times daily when creatinine clearance is 30-50 mL/min, and check renal function before starting.
- Contraindicated when creatinine clearance is **30 mL/min or less**; there is no safe reduced dose in severe renal impairment.
- Continue through a lapse rather than stopping, since benefit accrues over months and relapse is not a reason to discontinue.
- No taper is needed on stopping, and no hepatic dose adjustment is required at any stage of liver disease.

MECHANISM OF ACTION

- Structural analog of taurine and homotaurine that modulates glutamatergic transmission, with NMDA receptor modulation and mGluR5 antagonism proposed.
- Restores the glutamate-GABA balance disrupted by chronic alcohol, damping the hyperglutamatergic rebound that follows withdrawal.
- Reduces protracted withdrawal symptoms such as insomnia, anxiety, dysphoria and restlessness that commonly drive a return to drinking.
- Has no effect on alcohol reward or intoxication and produces no disulfiram-like reaction if the patient drinks.
- No action at opioid, dopamine, GABA-A or benzodiazepine receptors, so there is no sedation, euphoria or abuse liability.

PHARMACOKINETICS

- Oral bioavailability is only about **11%** and food reduces absorption further, yet dosing with meals is advised because it aids adherence.
- Not metabolized at all: the drug is excreted unchanged by the kidneys, so there is no hepatic clearance and no CYP450 involvement.
- Elimination half-life is **20-33 h**, with steady-state plasma concentrations reached after roughly 5 to 7 days of three-times-daily dosing.
- Supplied as enteric-coated delayed-release tablets that must be swallowed whole; crushing or chewing destroys the coating.
- Renal function alone governs exposure, which is why creatinine clearance drives every dose adjustment and the contraindication.

ADVERSE EFFECTS

- Diarrhea is the signature adverse effect, reported in roughly **10-17%**, usually mild, dose-related and improving after the first weeks.
- Nausea, flatulence, abdominal pain, pruritus, dry mouth and asthenia occur but rarely force discontinuation on their own.
- Anxiety, depression, insomnia and, uncommonly, suicidal ideation have been reported; the label calls for monitoring of mood.
- No hepatotoxicity, no sedation, no cognitive impairment and no abuse potential, which distinguishes it from most relapse-prevention options.
- Acute kidney injury and hypercalcemia have followed massive overdose; treatment is supportive with attention to calcium and renal function.
- Three-times-daily dosing and a large pill burden are the main practical causes of discontinuation rather than toxicity.

MONITORING

- Baseline serum creatinine with calculated creatinine clearance, repeated periodically and whenever the clinical picture changes.
- Screen for depression and suicidal ideation at each visit, since both alcohol use disorder and the drug label flag this risk.
- Track drinking days, heavy drinking days and craving with the timeline followback or AUDIT-C at every follow-up.
- Check adherence explicitly given the three-times-daily schedule; pill counts or pharmacy refill data are more reliable than self-report.
- Reassess overall benefit at 3 months and consider adding or switching to naltrexone, disulfiram or off-label topiramate if drinking persists.

INTERACTIONS & CAUTIONS

- No clinically significant drug interactions have been identified, because acamprosate is neither metabolized nor protein-bound to any degree.
- Studied without interaction alongside alcohol, diazepam, disulfiram and imipramine, so combination with these agents needs no dose change.
- Naltrexone raises acamprosate peak and total exposure, but the combination is well tolerated and no dose adjustment is recommended.
- Contraindicated in severe renal impairment, and caution is warranted with nephrotoxic agents such as NSAIDs or aminoglycosides.
- Safe to combine with antidepressants, antipsychotics and mood stabilizers, which makes it useful in complex psychiatric comorbidity.

SPECIAL POPULATIONS

- Pregnancy: animal data show skeletal malformations at high doses and human data are limited, so use only if the benefit clearly outweighs risk.
- Lactation: excretion into human milk is unknown; most authorities advise avoiding it or monitoring the infant closely if used.
- Pediatric safety and effectiveness have not been established and there is no established dose for patients under 18 years.
- Geriatric patients often have reduced creatinine clearance despite a normal creatinine, so calculate clearance before prescribing.
- Hepatic impairment requires no adjustment at any Child-Pugh class, making acamprosate the preferred agent in cirrhosis.

PRESCRIBING PEARLS

- Choose it when the goal is total abstinence and the liver is the problem; no hepatic dosing needed.
- Renal function is the only dose lever: cut to **333 mg TID** at CrCl 30-50, stop at 30 or less.
- Diarrhea early is expected and usually settles; do not abandon the drug in the first two weeks.

References

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Stahl, S. M. (2021). *Stahl's essential psychopharmacology: Neuroscientific basis and practical applications* (5th ed.). Cambridge University Press.

U.S. Department of Veterans Affairs & U.S. Department of Defense. (2021). *VA/DoD clinical practice guideline for the management of substance use disorders*. https://www.healthquality.va.gov/guidelines/MH/sud/

NOTE

References follow APA 7th edition style. Dosing, boxed warnings, and interaction data change; confirm every clinical decision against the current FDA prescribing information (DailyMed) and your institution's formulary. This sheet is an educational quick reference and does not replace the full label or clinical judgment.