Pharmacotherapy options for AUD

FIRST-LINE AUD PHARMACOTHERAPIES

The following table compares first-line AUD pharmacotherapies.

	Naltrexone	Acamprosate
Concurrent alcohol use	Can be used	Can be used
Contraindications	1. Any current opioid use (prescription or non-medical) 2. Acute opioid withdrawal 3. Acute hepatitis or liver failure	1. Severe renal impairment (creatinine clearance ≤ 30ml/min)
Cautions	1. Renal impairment 2. Severe hepatic impairment 3. Concomitant use of other potentially hepatotoxic drugs	1. Moderate renal impairment (creatinine clearance of 3050ml/min)
Side effects	• Nausea, headache and dizziness • Generally mild and temporary • Starting at low dose or abstinence can reduce side effects	• Diarrhea, vomiting and abdominal pain • Side effects are usually transient and resolve quickly
Coverage and cost	The cost of naltrexone and acamprosate will vary by coverage and jurisdiction. See the drug coverage table for details.	
Safety and other considerations	• Liver function tests (LFTs) at initial treatment and at 1, 3 and 6 months • More frequent monitoring if LFTs are elevated • Due to risk of hepatic injury, advise patients to stop treatment if signs of acute hepatitis appear (e.g., fatigue, anorexia, nausea and vomiting)	• No safety risk with mild renal impairment (creatinine clearance 50–80ml/min) • Moderate impairment (creatinine clearance 30–50ml/min) requires dose reduction • No hepatic toxicity
Dosing	Naltrexone can be prescribed as OD or PRN. PRN prescriptions are usually taken prior to drinking or when the patient is experiencing significant cravings. **Start:** 25mg OD for 1–2 weeks **Titrate:** to 50mg OD, if needed A slower titration may be indicated if intolerable GI symptoms or headache occur during initiation. Limited evidence suggests a higher dose of naltrexone may be safe, with safety and tolerability demonstrated at an increased dosage of 100–150mg/day. Dose may be increased to a maximum of 150mg per day if liver enzymes are within normal range and the patient is continuing to experience cravings at 50mg per day. Note that the product monograph recommends a dose of 50mg/day to treat AUD.	Motivation and treatment readiness may be particularly important factors for adherence, as due to its low bioavailability, acamprosate must be administered at a dosage of nearly 2g split into 3 doses per day. Start at maintenance dose: 2 x 333mg tablets TID

ALTERNATIVE PHARMACOTHERAPIES

This table offers information to support the selection of alternative pharmacotherapies. These can be used if first-line medications are contraindicated, not effective or not preferred.

	Topiramate	Gabapentin
Concurrent alcohol use	Can be used	• Safe to start while patients are using alcohol, but outcomes may be improved if patient has been abstinent for ≥ 3 days. • Abstinence is recommended after starting treatment due to potential risk of combined CNS-related side effects. If higher than average doses are used, observe patients carefully for CNS depression and adjust the dose of gabapentin as necessary.
Contraindications	1. Pregnant or planning to become pregnant 2. Narrow angle glaucoma 3. Nephrolithiasis	
Cautions	1. Concomitant use of valproic acid 2. Conditions or therapies that predispose patients to acidosis (e.g., renal disease, severe respiratory disorders, status epilepticus, diarrhea, surgery, ketogenic diets, certain drugs)	1. Concomitant use of opioids and other CNS depressants 2. Compromised respiratory function 3. Neurological disease or cognitive impairment 4. Renal impairment
Side effects	• CNS-related: psychomotor slowing, difficulty concentrating, speech/language problems, somnolence, fatigue, and mood disturbance. • Most side effects are mild to moderate in severity and occur early in treatment. • Start at low dose and titrate up to a stable dose over several weeks to avoid or reduce severity of side effects.	• Side effects include ataxia, slurred speech, and drowsiness. • Most side effects are mild to moderate in severity and occur early in treatment.
Coverage	The cost and coverage of topiramate and gabapentin vary by jurisdiction. See the drug coverage table for details.	
Safety and other considerations	• Due to risk of fetal harm, advise people of childbearing potential to use effective contraceptive. • No safety risk with liver disease. • Monitor for signs of hyperammonemia (e.g., unexplained vomiting, lethargy, confusion, changes in mental status, hyperthermia) and metabolic acidosis (hyperventilation, fatigue, anorexia, cardiac arrhythmias, stupor).	• Patients with compromised respiratory function, respiratory or neurological disease, renal impairment and older adults are at higher risk of experiencing severe adverse effects on the CNS. • Prescribe cautiously to older adults and those with renal or cognitive impairment, and provide close follow up. Do not prescribe to actively delirious patients. • Safe to use in patients with liver disease. • Dosage adjustment may be required with older adults and patients with renal impairment. • Prescribers should review gabapentin's drug–drug interactions when considering this medication as treatment for AUD. • Assess for non-medical use, diversion or dependency. • If gabapentin is stopped, withdrawal symptoms may occur.

<table>
<tr><th></th><th>Topiramate</th><th>Gabapentin</th></tr>
<tr>
<td>Sample dosing protocol</td>
<td>

Some individuals experience significant side effects, particularly at higher doses or with more rapid increases in dosage.
Gradual dose titration over several weeks is strongly recommended (e.g., approximately 4–8 weeks to full dose).
The recommended initial target dose for topiramate monotherapy in adults is 100mg/day, administered in 2 divided doses, as needed and tolerated.

<table>
<tr><th>Week</th><th>Morning Dose</th><th>Evening Dose</th></tr>
<tr><td>Week 1</td><td>None</td><td>25mg</td></tr>
<tr><td>Weeks 2–3</td><td>25mg</td><td>25mg</td></tr>
<tr><td>Weeks 3–4</td><td>50mg</td><td>50mg</td></tr>
</table>

If doses above 100mg/day are required, the dosage may be increased at weekly intervals in increments of 50mg up to a maximum of 400mg/day.
Increases over 100mg/day should be performed in specialist settings.
Studies have demonstrated better safety and tolerability of topiramate at lower doses (50–100mg/day), with side effects increasing at higher doses.
Dose and titration rate should be guided by side effects and clinical outcome. Some patients may benefit from a slower titration schedule or smaller increments in dose.
Daily doses above 400mg have not been adequately studied.

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<table>
<tr><td>Start</td><td>100–300mg TID</td></tr>
<tr><td>Titrate</td><td>If patient experiences anxiety or cravings, PRN to 1,800mg max daily.</td></tr>
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If patient continues to experience insomnia, a higher HS dose may be warranted.

Note: This protocol applies to immediate-release (IR) tablets.
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<tr><td></td><td colspan="2">Abbreviation: TID – 3 times per day, PRN – as needed/when necessary, HS – at bedtime</td></tr>
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