Appendix B: Pharmacotherapy for Alcohol Use Disorder

Generic Name *Trade name* Dosage form and strengths Concurrent alcohol use	Recommended Adult Dose[A]	Approx. Cost per month[B]	PharmaCare Coverage[C]	Adverse Effects[D]	Therapeutic Considerations
First line agents[4] • Naltrexone recommended for patients who have treatment goal of either abstinence or a reduction in alcohol consumption • Acamprosate is recommended for patients who have a treatment goal of abstinence					
Naltrexone *Revia, G* Tabs: 50 mg **Concurrent alcohol use**: Safe to start while using alcohol, may ↑ effectiveness ↓ adverse events if started 3-7 days abstinence[4] Note: IM naltrexone is not available in Canada	**Initial**: 12.5 - 25 mg PO daily x 1-2 weeks **Usual/Target**: 50 mg PO daily **Maximum**: 100 mg PO daily.[4] Administration: May begin treatment while patient is still drinking. Treatment should not be attempted until patient has remained opioid-free for 7-10 days. 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.[11,12] Dose may be increased to a maximum of 150mg per day if liver enzymes are within normal range and patient is continuing to experience cravings at 50mg per day.	$100	Regular benefit	Most common: nausea, headache, dizziness Other: sleep disturbances, decreased appetite, abdominal pain, elevated liver enzymes (dose related) ADRs are generally mild, subside over time, may be avoided if naltrexone started at lower dose and/or if patient is abstinent from alcohol[4] Acute hepatitis or liver failure: Naltrexone has capacity to cause dose related hepatocellular injury. Prior to treatment, clinician should establish whether patient has subclinical liver injury or disease.[1]	Efficacy:[4] • NNT = 20 to prevent return to any drinking (relapse) • NNT = 12 to prevent return to heavy drinking Contraindications: • Naltrexone hypersensitivity • **Current opioid use, including prescribed opioids (e.g., opioid agonist treatment) or illicit opioids** • Acute hepatitis or liver failure Monitoring: • LFTs at initiation, 1 mo, 3 mo and 6 mo. More frequent monitoring if LFTs elevated Short term opioid use: • If opioid pain management is anticipated (e.g., elective surgery), discontinue oral naltrexone ≥ 3 days prior to surgery.[2] Patient counselling: • Patients should be aware that they may be more sensitive to lower doses of opioids after discontinuation of naltrexone. • Due to risk of hepatic injury, advise patients on signs of acute hepatitis and to stop treatment if symptoms appear

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Acamprosate *Campral* Tabs: 333 mg **Concurrent alcohol use**: Safe to start while using alcohol, may ↑ effectiveness if started 3-7 days abstinence[4]	**Initial/Usual/Max**: 666 mg PO three times per day	$160	Regular benefit	Most common: diarrhea Less common: vomiting, abdominal pain Usually transient and resolve quickly Rare: suicidal ideation	Efficacy:[4] • NNT = 12 to prevent return to any drinking (relapse) • Not associated with improvement in alcohol consumption Contraindications: • Acamprosate hypersensitivity • Severe renal impairment CrCl ≤ 30 mL/min • Nursing women
Second line agents					
Topiramate *Topamax, G* Tabs: 25, 50, 100, 200 mg Sprinkle cap: 15, 25 mg **Concurrent alcohol use**: Safe to start while using alcohol	*Off-label* **Week 1**: 25 mg PO PM **Week 2-3**: 25 mg PO BID **Week 3-4**: 50 mg PO BID **Max**: 400mg/d Gradual dose titration to reduce AE. If doses above 100mg/d are required, may increase 50mg/d weekly.	$15-45	Regular benefit	Most common: psychomotor slowing, difficulty concentrating, speech problems, somnolence, fatigue, irritability, depression Adverse effects more likely with higher doses or with rapid increases in dosage[3]	Efficacy:[4] • 7 RCTs reported small to moderate effects on abstinence and heavy drinking outcomes compared to placebo • 3 trials reported topiramate is as effective or superior to naltrexone for abstinence, heavy drinking and craving outcomes Contraindications:[4] • Topiramate hypersensitivity • Pregnant or planning to be pregnant • Narrow angle glaucoma • History of nephrolithiasis

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Gabapentin *Neurontin, G* Caps: 100, 300, 400, 600, 800 mg **Concurrent alcohol use**: Safe to start while using alcohol. May be better outcomes if started ≥ 3 days abstinent.[4]	*Off-label* **Initial**: 100-300 mg PO TID **Max**: 1800mg/d Abrupt withdrawal is not recommended due to possibility of increased seizure frequency. Gradual reduction is recommended.[1]	$20	Regular benefit	Most common: dizziness, ataxia, slurred speech, drowsiness, peripheral edema Physiological dependence: • noted only among patients with history of alcohol, stimulant or opioid use disorder and average daily dose ~3000 mg/d (range 600-8000 mg/d) Withdrawal symptoms: • restlessness, disorientation, confusion, agitation, anxiety • does not resolve with administration of benzodiazepines • occurred within 12 hours to 7 days of discontinuation	Efficacy:[4] • 3 RCTs reported small to moderate effects on abstinence and heavy drinking outcomes, craving, mood and insomnia compared to placebo • One RCT (long-acting formulation) found no difference in alcohol consumption or craving compared to placebo Contraindication: • Gabapentin hypersensitivity Drug interactions: • Concomitant use of gabapentin with opioids and other CNS depressants may result in respiratory depression, profound sedation, syncope and death[1] Potential for non-medical use: • diversion, using higher doses, combining with other substances to potentiate euphoric effects, inhaled, injected or other routes • documented among opioid using populations and in facilities where access to alcohol and other drugs is restricted (e.g., inpatient treatment programs, correctional facilities)[4] Recommend: • Abstinence recommended after starting treatment to ↓ risk of CNS adverse effects • If diversion or misuse is a concern, prescriber can consider daily, weekly or biweekly dispense from a pharmacy, or blister packing with random pill count checks.

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Disulfiram *Compounded product* *Antabuse is discontinued* **Concurrent alcohol use**: contraindicated. Must be abstinent at least ≥ 12 h	**Initial/Usual**: 250 mg PO daily **Max**: 500 mg PO daily Commercial product cancelled post marketing. Available only through specialty compounding pharmacies.	Call pharmacy $50	Regular benefit	Absence of alcohol, most common side effects: drowsiness, skin eruptions (acne, dermatitis), fatigue, erectile dysfunction, headache, metallic/garlic after taste Severe but less common: hepatotoxicity Presence of alcohol: Causes disulfiram reaction when combined with alcohol. Symptoms are proportion to amount of alcohol consumed. Not recommended	Efficacy:[4] • 5 RCTs reported disulfiram no more effective than placebo in supporting abstinence or preventing relapse • 2014 meta-analysis concluded disulfiram is effective in supporting abstinence if administered under structured and supervised conditions Contraindications: • Concurrent or recent use of metronidazole or alcohol • Alcohol intoxication • Severe myocardial disease, coronary occlusion • Active psychosis Drug interactions: • warfarin, isoniazid, metronidazole, phenytoin Not commonly used due to adverse effects. Not recommended except in specific circumstances for highly motivated patients Recommend patients carry an identification card listing symptoms of disulfiram alcohol reaction and contact information in cases of emergency

Abbreviations: **CAP** capsules; **CrCl** creatinine clearance; **G** generics; **LFT** liver function tests; **mo** month; **Tab** tablets.

[A] For normal renal and hepatic function. Consult product monograph for detailed dosing instructions and dose adjustments for unique patient populations

[B] Drugs costs are average retail cost of the generic, when available. Current as of Feb 2022 and does not include retail markups or pharmacy fees.

[C] PharmaCare coverage as of Feb 2022 (subject to revision). Regular Benefit: Eligible for full reimbursement*. Limited Coverage: Requires Special Authority to be eligible for reimbursement*. Non-benefit: Not eligible for reimbursement. *Reimbursement is subject to the rules of a patient's PharmaCare plan, including any deductibles. In all cases, coverage is subject to drug price limits set by PharmaCare. See: www.health.gov.bc.ca/pharmacare/plans/index.html and www.health.gov.bc.ca/pharmacare/policy.html for further information.

[D] Not an exhaustive list. Check the product monograph (https://health-products.canada.ca/dpd-bdpp/index-eng.jsp) or an interaction checker (e.g., Lexicomp(c)) before prescribing

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