Appendix A: Pharmacotherapy Options for Outpatient Management of Alcohol Withdrawal

Generic Name *Trade name* Dosage form and strengths Concurrent alcohol use	**Recommended Adult Dose**[A]	**Approx. Cost per course**[B]	**PharmaCare Coverage**[C]	**Adverse Effects**[D]	**Therapeutic Considerations**
Anticonvulsants					
Carbamazepine *Tegretol, G* IR Tabs: 200 mg Chewable: 100, 200 mg ER tab: 200, 400 mg Oral suspension: 20 mg/mL **Concurrent alcohol use**: no safety risk	IR tabs: Day 1: 200 mg QID Day 2: 200 mg TID Day 3: 200 mg BID Day 4-5: 200 mg once daily[4]	$3	Regular benefit	Dizziness, pruritis, ataxia, headache, drowsiness and nausea (all usually minor and temporary)	Efficacy:[4] • 6 RCTs report equal or superior efficacy in reduction of withdrawal symptom severity compared to benzodiazepines • Insufficient evidence for prevention of seizures or delirium tremens Contraindications:[4] • Hepatic disease • Bone marrow depression • Serious blood disorder • Atrioventricular heart block Caution: • The HLA-B*15:02 and HLA-A*31:01 alleles increase risk of carbamazepine toxicity. Consider monitoring patients for adverse reactions (SJS, TEN, maculopapular rash) if there is an elevated risk of carrying these alleles. • People of Asian descent are at increased risk of serious cutaneous adverse drug reactions (Stevens-Johnson Syndrome, Toxic Epidermal Necrolysis [TEN], maculopapular rash) due to a higher baseline prevalence of the HLA-B*1502 allele, a marker for carbamazepine toxicity. Avoid carbamazepine in this population unless genetic testing is available and has excluded risk. Other: • Considerations for use: non-sedating, no interaction with alcohol, no reported potential for non-medical use or diversion • Some adverse effects resemble withdrawal symptoms; ascertain the source of symptoms before dose adjustments • Baseline and periodic evaluations of hepatic function must be performed in elderly patients or patients with history of liver disease

Generic Name *Trade name* Dosage form and strengths Concurrent alcohol use	Recommended Adult Dose[A]	Approx. Cost per course[B]	PharmaCare Coverage[C]	Adverse Effects[D]	Therapeutic Considerations
Gabapentin *Neurontin, G* Caps: 100, 300, 400 mg Tabs: 600, 800 mg **Concurrent alcohol use**: Safe to start while using alcohol. Abstinence is recommended.[4]	**Day 1** Daytime dose: 300mg TID Evening dose: 600-1200mg HS PRN dose: 300mg PRN Total daily dose: Up to 2400mg **Day 2-3** Daytime dose: Titrate quickly as tolerated: 600mg TID Evening dose: 600-1200mg HS PRN dose: If symptoms persist: Additional 300mg TID PRN + 600–1200mg HS PRN Total daily dose: Up to 3600mg **Day 4** Daytime dose: When symptoms resolve, taper to 600mg TID Evening dose: 600-900mg HS PRN dose: NA Total daily dose: Up to 2700mg **Day 5** Daytime dose: Taper to zero over next 3-5 days by 600mg per day 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	Efficacy:[4] • 2 RCTs report gabapentin (1200 mg/d) is as effective as benzodiazepines in suppressing mild to moderate withdrawal symptoms • May be superior to benzodiazepines for treating insomnia and anxiety symptoms • Insufficient evidence for prevention of seizures or delirium tremens. Contraindication: • Gabapentin hypersensitivity Drug interactions: • Use with opioids may result in respiratory depression, profound sedation, syncope and death[1] Abstinence recommended after starting treatment to ↓ risk of CNS adverse effects 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] 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

Generic Name *Trade name* Dosage form and strengths Concurrent alcohol use	Recommended Adult Dose[A]	Approx. Cost per course[B]	PharmaCare Coverage[C]	Adverse Effects[D]	Therapeutic Considerations
Alpha adrenergic agonists					
Clonidine *G* Tabs: 0.025, 0.1, 0.2 mg **Concurrent alcohol use**: additive effect on lowering blood pressure. Patients and family may receive education on signs and symptoms of hypotension	**Initial**: 0.1-0.2 mg BID (last dose HS) **Titrate**: Can add 0.2 mg daily if needed **Final**: 0.1-0.6 mg BID[4] May also be considered as an adjunct to carbamazepine, gabapentin or other anticonvulsants.	$3	Regular benefit	Hypotension, dry mouth, dizziness, fatigue, headache, nausea, vomiting, constipation, malaise, sleep disorder, sedation, erectile dysfunction	Efficacy:[4] • 2 RCTs reported clonidine was as effective as benzodiazepines in reducing mild to moderate withdrawal symptoms • Does not prevent seizure or delirium tremens Contraindications: • Sinus node function impairment • Severe bradyarrhythmia • Galactose intolerance Other: • Use for treating mild-moderate withdrawal symptoms in patients at low risk of severe complications • Centrally acting alpha-2 adrenergic agonist that can suppress persistent noradrenergic symptoms (e.g., hypertension, tachycardia) • Safe to use as adjunct to benzodiazepines or other anticonvulsants (no reported safety issues and can manage withdrawal symptoms via different mechanism of action) • Patients should receive education on signs and symptoms of hypotension

Generic Name *Trade name* Dosage form and strengths Concurrent alcohol use	Recommended Adult Dose[A]	Approx. Cost per course[B]	PharmaCare Coverage[C]	Adverse Effects[D]	Therapeutic Considerations
Benzodiazepines					
Diazepam *Valium, G* Tabs: 2, 5, 10 mg **Concurrent alcohol use**: potentiates the effects of alcohol, can result in serious safety risks e.g., over sedation, falls, delirium, respiratory depression, need for prolonged hospitalization	Day 1: 5-10 mg QID Day 2: 5-10 mg TID Day 3: 5-10 mg BID Day 4: 5-10 mg HS[4]	$2	Regular benefit	Most common: drowsiness, dizziness Other: changes in skin colour, nausea, headache, blurred vision, tremors, hypotension, GI disturbances, memory loss	Efficacy:[4] • Results from a 2010 meta-analysis demonstrate superior efficacy in suppression of withdrawal symptoms compared to placebo and other active treatments • Results from 3 meta-analyses suggest superior efficacy for prevention of seizures compared to placebo and active treatments Contraindications: • Severe respiratory insufficiency (diazepam) • Severe hepatic impairment (diazepam) • Sleep apnea (diazepam) • Myasthenia gravis • Narrow angle glaucoma Other: • Lorazepam is preferred for those with severe respiratory or liver disease and in elderly (consider lower dosing) • Potential for non-medical use, diversion and dependence • Potential for drug-drug interactions leading to excess sedation, impaired psychomotor and cognitive functioning • Exercise caution for outpatient use **Short term use only. Limited to acute phase of alcohol withdrawal**
Lorazepam *Ativan, G* Tabs: 0.5, 1, 2 mg Sublingual tabs: 0.5, 1, 2 mg **Concurrent alcohol use**: potentiates the effects of alcohol, can result in serious safety risks e.g., over sedation, falls, delirium, respiratory depression, need for prolonged hospitalization	Day 1-2: 1-2 mg every 4h Day 3-4: 0.5-1 mg every 4h[4]	$3	Regular benefit		

Abbreviations: **CAP** capsules; **G** generics; **mo** month; **SJS** Stevens-Johnson syndrome **TEN** Toxic epidermal necrolysis **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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Pharmacotherapy Options for Outpatient Management of Alcohol Withdrawal

- Patients at high risk of severe complications of withdrawal (PAWSS ≥ 4) should be referred to an inpatient facility. (See Recommendation 6: Care Setting for Withdrawal Management in Patients at Low Risk of Severe Complications)
- BCCSU guidelines recommend non-benzodiazepine medications as the preferred approach for outpatient management.
  - Carbamazepine and gabapentin have been shown to be safe and effective for mild-moderate withdrawal symptoms compared to placebo.
  - Use of clonidine as an alternative or adjunctive option is also supported by moderate certainty evidence.
  - There is insufficient evidence that gabapentin, carbamazepine and clonidine are effective for preventing seizures or delirium tremens.
- Limited evidence for valproic acid, should only be used when all other pharmacotherapy options are contraindicated
- Benzodiazepines not a preferred option for outpatient withdrawal management due to side effects, potentiation of alcohol effects, and potential non-medical use and dependence.
- If they are prescribed for outpatient management, following measures should be considered:
  - Short course (3-7d) with fixed-dose schedule
  - Daily dispense from a pharmacy
  - Frequent clinical visits to closely monitor adverse effects, symptoms, alcohol use and make dose adjustments as needed.
- For additional details, please refer to section 5 and pharmacotherapy tables available at BCCSU guidelines