Drug Table: Naltrexone and Acamprosate for Alcohol Use Disorder

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	Naltrexone	Acamprosate
Mechanism of action	• Known opioid-receptor antagonist. • Reduces the urge to drink, as well as interfere with the desire to continue drinking if alcohol is consumed. • Not associated with tolerance or dependence.	• Possible glutamate receptor antagonist. • Restores balance between neuronal excitation and inhibition that becomes altered by chronic alcohol exposure; reduces symptoms associated with post-withdrawal (i.e., sleep and mood disturbances). • Not associated with tolerance or dependence.
Dose	• Standard daily dose: 50 mg (1 x 50 mg tablet) orally daily • Dose titration: 25 mg for first few days to help with GI tolerability. *NOTE: If patients are physically dependent on opioids this medication will precipitate withdrawal.*	• Standard daily dose: 666 mg (2 x 333 mg tablets) orally TID • Dose titration: 333 mg TID for first few days to help with GI tolerability. • Dose adjustments for renal impairment: ○ Moderate (CrCL 30-50 mL/min): 333 mg TID is recommended. ○ Severe (CrCL 30 mL/min or less): *Contraindicated.*
Place in Therapy	• Most effective to help reduce heavy drinking. • Small, uncertain effects to support abstinence (return to any drinking).	• Most effective to support abstinence (return to any drinking). • Generally, not recommended to help reduce heavy drinking.
	Studied in conjunction with psychosocial interventions; should be offered/encouraged as combination therapy. Current evidence does not suggest added benefit when naltrexone and acamprosate are combined.	
Treatment Initiation	• Safe to start while patients are using alcohol but may be more effective if started following a few days of abstinence. • Start in patients who are *opioid free* (7-14 days) because naltrexone can precipitate or exacerbate opioid withdrawal symptoms. ***Local Clinical Expert Opinion***: Naltrexone may be considered in individuals with a history of opioid use disorder who have been abstinent from opioids for 6 months or longer. • Naltrexone is associated with a reduced tolerance to opioids. Patients should be made aware of the potential risk.	• Safe to start while patients are using alcohol but may be more effective if started following completion of withdrawal management.
Treatment Duration	A specific treatment duration has not been well established. Guidelines recommend at least 6 months then reassess. ***Clinical Practice Guidelines*** ***Local Clinical Expert Opinion:*** • Medications should be prescribed for a minimum of 3 months. • If the patient is achieving treatment goals, the medication may be continued to support recovery with ongoing monitoring for up to 2 years. • If the medication, as a tool is helping, individuals may choose to continue longer term.	

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Common Adverse effects	• Nausea, vomiting, abdominal pain, anxiety, insomnia, nervousness, fatigue, dizziness, joint and muscle pain, and headache.	• Diarrhea, nausea, vomiting, abdominal pain.
	Adverse reactions usually occur early during drug therapy and are transient. Dose titration minimizes side effects.	
Drug interactions	• Opioids • Caution with other potentially hepatotoxic medications	• None reported
Contraindications	• History of sensitivity to naltrexone • Any current opioid use (analgesia, opioid agonist treatment, or non-medical use) or acute opioid withdrawal • Acute Hepatitis or Liver Failure	• History of sensitivity to acamprosate • Severe renal impairment (CrCL of 30mL/min or less) • Breastfeeding*
Precautions	• Renal impairment: Use with caution as naltrexone and its primary metabolite is excreted through the urine. • Breastfeeding* • Pregnancy* • Hepatotoxicity: Naltrexone has been associated with variable rates of serum enzyme elevations. No cases of hepatic failure have been reported. Advise patients of signs of acute hepatitis (i.e., fatigue, anorexia, nausea, vomiting) and to stop treatment if they appear.	• Moderate renal impairment (see "dose" section for dosage adjustments) • Pregnancy*
Lab Monitoring	• Liver function should be checked prior to initiation, or within several weeks of starting treatment, and monitored periodically (e.g., every 3 - 6 months). ***Clinical Practice Guidelines*** ○ Choosing Wisely Canada recommends not waiting for liver enzyme results to initiate naltrexone. There is little evidence of hepatotoxicity at standard doses (50 mg once daily) and delaying initiating therapy may result in patients being lost to care** ○ Increased monitoring is advised in hepatic impairment.	• Renal function tests (urea/electrolytes/serum creatinine)
Cost/30 days* **	$84 (50 mg daily) ***generics available***	$163 (666 mg TID)
Nova Scotia Pharmacare Status	Full benefit	Full benefit

This document is not intended to be all-inclusive. Please refer to the Health Canada Product Monographs and the Academic Detailing document "Alcohol Use Disorder: First-Line Pharmacotherapy 2024" available at https://medicine.dal.ca/departments/core-units/cpd/programs/academic-detailing-service/AC-Service-Resources.html for more information and references. TID = three times daily; CrCL = creatinine clearance
Safety and efficacy have not been well established in these patient populations ** https://choosingwiselycanada.org/recommendation/addiction-medicine/ * Pricing is approximate from www.mckesson.ca*
***Clinical Practice Guidelines**: British Columbia Centre on Substance Use (BCCSU), 2019, available at: https://www.bccsu.ca/clinical-care-guidance/.*