Pharmacotherapy for Alcohol Use Disorder

Addiction Day—CSAM
November 12, 2015
Banff Alberta

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Certificant International Society of Addiction Medicine
Diplomate American Board of Addiction Medicine
No conflicts of interest to declare

- **Background:**
  - Alberta Health Services
    - Foothills Medical Centre Addiction Centre
    - Addiction Network Hospital Consults
    - Renfrew Recovery and Detox Centre
    - Opioid Dependence Program
  - C.U.P.S. Primary Care Clinic
  - Clinical Assistant Professor Department of Family Medicine University of Calgary

- Board Member Canadian Society of Addiction Medicine; CSAM—SCMA
Outline

- Pharmacotherapy options for treatment of alcohol use disorder (AUD)
  - Naltrexone
  - Acamprosate
  - Disulfiram
  - Others?

- Mechanisms of action

- Current evidence

- Dosing and initiation, contraindications, side effects, monitoring

- Cost and availability

- Cases
## Medication options

- **3 Medications approved by Health Canada\(^1\):**
  - Naltrexone
  - Acamprosate
  - Disulfiram

- **Numerous off-label medications, some requiring further study:**
  - Moderate evidence for Topiramate, Nalmefene,\(^2\)
  - Limited evidence for Gabapentin,\(^3\) Baclofen\(^4,5\)

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\(^3\) Uptodate. Pharmacotherapy for alcohol use disorder. 2015.


Medication options

- Underutilized
  - <1/3 of those with AUD receive treatment\(^1\) and <10% with AUD receive pharmacotherapy\(^2\)
  - Should be considered for all patients with moderate or severe alcohol use disorder\(^2,3,4,5,6\) who:
    - Have current, heavy use and ongoing risk for consequences\(^4\)
    - Motivated to reduce intake\(^4\)
    - Prefer medication along with (ideally) or instead of psychological intervention\(^4\)
    - Have no medical contraindications to the drug\(^4\)

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1 Hasin D, Stinson F, Ogburn E, Grant B. Prevalence, correlates, disability, and comorbidity of DSM-IV alcohol abuse and dependence in the United States: results from the National Epidemiologic Survey on Alcohol and Related Conditions. ArchGen Psychiatry. 2007;64(7):830-842.
4 Uptodate. Pharmacotherapy for alcohol use disorder. 2015.
Medication options

- Modeling study estimated that if 40% of all individuals with alcohol use disorder mod-severe received pharmacotherapy, there would be a 13% reduction in alcohol-attributable mortality in the European Union\(^1\)

- Barriers:
  - Cost?
  - Availability?
  - Prescriber and treatment team familiarity and support?
  - Education re: effectiveness?

Mechanism of action

<table>
<thead>
<tr>
<th>Naltrexone</th>
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</thead>
<tbody>
<tr>
<td>Opioid receptor antagonist</td>
</tr>
<tr>
<td>Reduces rewarding effects of ETOH, by reducing dopamine release in response to ETOH&lt;sup&gt;1&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

- May be particularly effective in those with genetic susceptibility<sup>2</sup>
  - Asp variant of the OPRM 1 gene less likely to relapse
  - Heterozygotes for ASP-40 allele 6x more favourable outcome

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<sup>2</sup> Uptodate. Pharmacotherapy for alcohol use disorder. 2015
Mechanism of action

**Acamprosate**

Restores the balance between GABA and glutamate systems disrupted by chronic alcohol use. Thought to normalize hyper excitability and re-establish homeostasis.¹,²

² Restrepo R. Diagram adapted from ASAM Review Course 2015.
Mechanism of action

Disulfiram

Blocks conversion of acetaldehyde to acetic acid, causing buildup acetaldehyde.¹

Mechanism of action

- **Topiramate**
  - Combination of potential mechanisms: Blocks neuronal voltage-dependent sodium channels, enhances GABA\textsubscript{A} activity, resulting in inhibitory effect\textsuperscript{1}

- **Gabapentin**
  - Structurally related to GABA but doesn’t activate GABA\textsubscript{A} or GABA\textsubscript{B}. Instead may bind to sites which correspond with voltage-gated calcium channels with the alpha-2-delta-1 subunits. These channels are located presynaptically, and may modulate the release of excitatory neurotransmitters\textsuperscript{1}

- **Baclofen**
  - Activates GABA\textsubscript{B}, blocks monosynaptic and polysynaptic reflexes by acting as an inhibitory neurotransmitter, blocking the release of excitatory transmitters\textsuperscript{1}

- **Nalmefene**
  - Adopted in Europe but is not available in NA
  - Similar to naltrexone in structure and activity—opioid antagonist—but longer half life, greater bioavailability, more effective binding to central opioid receptors and no observed dose-dependent liver toxicity\textsuperscript{2}

\textsuperscript{1} Uptodate. Drug Information, 2015
\textsuperscript{2} Uptodate. Pharmacotherapy for alcohol use disorder. 2015
Outcomes

- Abstinence
  - Return to any drinking: Yes/No

- Reduction in consumption
  - Return to any heavy* drinking: Yes/No
  - % drinking days
  - % heavy drinking days

* ≥5 for males or ≥4 females
Evidence

Original Investigation

Pharmacotherapy for Adults With Alcohol Use Disorders in Outpatient Settings
A Systematic Review and Meta-analysis

Daniel E. Jonas, MD, MPH; Halle R. Amick, MSPH; Cynthia Feltner, MD, MPH; Georgiy Bobashev, PhD; Kathleen Thomas, PhD; Roberta Wines, MPH; Mimi M. Kim, PhD; Ellen Shanahan, MA; C. Elizabeth Gass, MPH; Cassandra J. Rowe, BA; James C. Garbutt, MD

CONCLUSIONS AND RELEVANCE  Both acamprosate and oral naltrexone were associated with reduction in return to drinking. When directly compared with one another, no significant differences were found between acamprosate and naltrexone for controlling alcohol consumption. Factors such as dosing frequency, potential adverse events, and availability of treatments may guide medication choice.

Naltrexone po and Acamprosate associated with improved consumption outcomes

- Abstinence rates compared to placebo
  - Both acamprosate and naltrexone po showed fewer returned to drinking (9% and 5% fewer respectively):
  - Inadequate evidence in well-controlled trials or no benefit for other medication options

- NNT to prevent return to any drinking (abstinence)
  - Acamprosate: 12
  - Naltrexone po: 20

- Return to heavy drinking compared to placebo
  - Acamprosate=no improvement
  - Naltrexone po=improvement with NNT: 12
    - 9% fewer returned to heavy drinking
  - Inadequate evidence in well-controlled trials or no benefit for other medication options

Naltrexone po and Acamprosate associated with improved consumption outcomes¹

- % drinking days compared to placebo
  - Both acamprosate and naltrexone po showed reductions (8.8% and 5.4% respectively)
  - Disulfiram: No statistically significant difference
  - Some evidence for topiramate as discussed below

- % heavy drinking days
  - Both acamprosate and naltrexone po showed reductions (2.6% and 4.1% respectively)
  - Disulfiram: No well-controlled trials looking at this
  - Some evidence for topiramate & nalmefene as discussed below

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Naltrexone po and Acamprosate associated with improved consumption outcomes

- "Meta-analyses of head-to-head RCTs comparing acamprosate with naltrexone po found no statistically significant difference between the two medications"
- COMBINE was one of the RCTs included
  - Naltrexone (+MM)* = Combined behavioural intervention (+MM)=Naltrexone+CBI (+MM)
  - All better than placebo
  - But acamprosate showed no evidence of efficacy over placebo with or without CBI

NALTREXONE AND ACAMPROSATE ARE CONSIDERED 1ST LINE

* Medical management: comprised of up to 9 manual-guided counselling visits at weeks 0,1,2,4,6,8,10,12 &16. Initial visit 45mins; 20 mins thereafter. Includes advice for reducing ETOH, review of adverse effects of meds., & emphasis on importance of adherence.

Acamprosate vs. Naltrexone?

- No statistically significant difference for return to any drinking (abstinence) or reduced consumption—both equally effective\(^1\)
- Earlier studies suggested\(^2,3,4\)
  - Acamprosate: more effective for abstinence, +anxiety
  - Naltrexone: more effective for ↓ heavy use, strong cravings

- Factors such as dosing regimen, potential adverse events, preference, cost and availability may guide selection

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\(^2\) Uptodate. Pharmacotherapy for alcohol use disorder. 2015


Depot Naltrexone?

- Not available in Canada

- Systematic review and meta-analysis found:
  - Association with reduction in heavy drinking days
    - 4.6% reduction\(^1\)
    - 25% greater reduction in heavy drinking days than placebo at 24wks\(^2\)
  - No association with abstinence, or return to heavy drinking (whereas naltrexone po shows benefit)\(^1\)
    - Insufficient data? Benefit of daily po ritual?
  - Depot may improve adherence and achieve steady therapeutic level of medication (reducing peak adverse events)\(^2\)

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2 Uptodate. Pharmacotherapy for alcohol use disorder. 2015
Moderate evidence for topiramate and nalmefene

- **Topiramate:**
  - No strong evidence supporting improved abstinence
  - 6.5% fewer drinking days
  - 9% fewer heavy drinking days
  - 1% fewer drinks per drinking day
  - Off label

- **Nalmefene:**
  - No strong evidence supporting improved abstinence
  - 2% fewer heavy drinking days
  - 1% fewer drinks per drinking day
  - One of the larger studies in the meta-analysis showed:
    - 44% Reduction in mean number of heavy drinking days in nalmefene group compared to on 32% reduction in placebo
  - Off label

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2 Uptodate. Pharmacotherapy in alcohol use disorder. 2015.
Gabapentin?

- May have efficacy for improving abstinence rates and improved rates for no heavy drinking, although not definitively established with large enough sample size\(^1\)
  - At 12 weeks abstinence rates 11% for Gabapentin 900mg/day; 17% for 1800mg/day vs. 4% in placebo (all had manual-based counseling); 150 patients\(^2\)
  - Earlier trial shows reduced consumption but small sample sizes and other methodological limitations\(^1\)
- Off label

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1 Uptodate. Pharmacotherapy for alcohol use disorder. 2015.
Baclofen?

- There is some evidence for the use of baclofen
  - Two 12-wk trials\(^1,2\) with total of 123 patient showed improved abstinence vs. placebo (71% and 70% with baclofen respectively vs. 29% and 21% with placebo respectively)
  - One 12-wk trial\(^3\) with 80 patients so no differences in abstinence, HDD, or time to relapse
  - Preliminary results from a retrospective case series and a secondary analysis of clinical-trial data suggest higher dose (60mg vs. 30mg) may be effective\(^4\)
  - Off label AND evidence weak at present

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\(^4\) Uptodate. Pharmacotherapy for alcohol use disorder. 2015.
Disulfiram

- Controversy regarding efficacy
- Numerous studies showing both positive and negative outcomes
Unsupervised vs. supervised disulfiram

- Unsupervised: patient takes on own
- Wide range of definitions for supervision
  - Ranging from a administration by a family member to intensive daily supervised administration and counselling at outpatient treatment centres
Disulfiram—Evidence?

- **2010 Review**
  - Overall positive results for abstinence and reduced consumption
  - Variety of supervised and unsupervised settings

- **2011 Systematic review and meta-analysis**
  - No effect of *unsupervised* disulfiram on abstinence compared to placebo at 1 year
  - Greater effectiveness for *supervised* disulfiram compared to none or other treatments at 2 and 12 months

**BUT**

applicability of conclusions for those 2 reviews?

- In the 2010 review\(^1\) 4/7 positive studies were done by De Sousa et al. and 4/5 studies showing superiority for disulfiram were done by De Sousa et al.

- Similarly, the 2011 systematic review and meta-analysis\(^2\) was weighted heavily by the De Sousa studies

- Setting for De Sousa studies\(^3,4\):
  - India; same research team
  - Mostly joint rather than nuclear families
  - Typically >1 family member monitoring medication
  - Consumption <4 drinks per day was not included

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2014 Systematic review and meta-analysis\textsuperscript{1} —unsupervised disulfiram only

- Evidence from well-controlled studies does NOT adequately support an association with:
  - Improved abstinence
  - Reduction in return to heavy drinking
  - Decreased % heavy drinking days
  - Decreased drinks per drinking day

Minimally Supervised Disulfiram

- Subgroup analysis of the largest disulfiram trial\(^1\)—Fuller et al. 1986, RCT; Veterans Administration Cooperative study\(^2\)
  - *May reduce drinking frequency (% drinking days) after relapse in subset (older more socially stable men who relapse)*\(^2\)

- Yoshimura et al. 2014, RCT\(^1\); Disulfiram 200mg daily
  - Supervision by spouse or relative
  - Intervention of letters mailed to inform patients of harmful effects of alcohol, coping with cravings, methods to maintain abstinence by using disulfiram
  - No benefit for total abstinence; Insufficient data to measure reduced consumption

- Ulrichsen et al. 2010, RCT\(^2\); Disulfiram 800mg 2x/week
  - Supervised twice weekly by RN + CBT 16 sessions over 26 weeks
  - No benefit for total abstinence; Non statistically significant *trend towards increased abstinent days* or reduced consumption

- Niederhofer and Staffen 2003\(^3\); Disulfiram 200mg daily
  - No benefit for total abstinence; *Increased abstinent days* or reduced consumption
  - Very small sample

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Disulfiram effective for abstinence in intensive, long-term, biopsychosocial therapeutic approach to alcohol use disorder

Outpatient Long-term Intensive Therapy for Alcoholics (OLITA): a successful biopsychosocial approach to the treatment of alcoholism


Supervised Disulfiram as Adjunct to Psychotherapy in Alcoholism Treatment

Henning Krampe¹,* and Hannelore Ehrenreich²
52% abstinent over 7 years post-tx follow-up.

High abstinence rates attributed to¹:

- Therapists making full use of the psychological actions of the drug
  - Deterrence:
    - Repeated explanation of the action of disulfiram (flushing, tachycardia, sweating, headache, nausea, mild dizziness)
    - Repetition of acquired information by the patient
  - Autosuggestion (internalized belief)
    - Feeling of protection due to taking
    - Real fear of ingesting alcohol
  - Therapeutic ritual with strict supervision to ensure ingestion
  - Frequently renewed active decision process
  - Continuous reinforcement of a sober lifestyle and development of new coping skills

Outpatient Long-term Intensive Therapy for Alcoholics (OLITA): a successful biopsychosocial approach to the treatment of alcoholism
Henning Krampe, PhD; Sabina Stawicki, PhD; Margret R. Hoehe, MD, PhD; Hannelore Ehrenreich, MD, DVM

“During psychoeducation, the therapist dramatically outlines the danger of drinking alcohol under the influence of disulfiram and passes responsibility onto the patient, even asking for a promise to stop taking the medication before drinking. This information is followed by the supervised intake of the drug, establishing a therapeutic ritual. The patient is challenged each time to actively decide against alcohol and for sobriety in front of a witness. During this therapeutic ritual, the therapist praises the patient for taking disulfiram and for maintaining abstinence, thereby providing a continuous reinforcement of a sober lifestyle. Since drinking is no longer an option of problem-solving, one part of this new lifestyle is the development and training of alternative coping skills.”

Disulfiram conclusions for alcohol use outcome

- Weak evidence it *may* reduce drinking frequency (% drinking days) after relapse in subset (older more socially stable men who relapse)\(^1\)

- Does *NOT* appear to improve abstinence outcomes, supervised or unsupervised\(^2,3\)…..

- ….except possibly when used as *ADJUNCT* to intensive, long-term, biopsychosocial approach\(^4\)

\[= 2^{\text{ND}} \text{ LINE MEDICATION WITH LIMITED EVIDENCE — IS APPROVED BY HC FOR AUD}\]

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Acamprosate and naltrexone conclusions for alcohol use outcome

- Both improve abstinence
  - No statistically significant difference between them
- Both reduce consumption
  - No statistically significant difference between them

= 1\textsuperscript{st} LINE MEDICATIONS WITH BEST EVIDENCE— BOTH APPROVED BY HC

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Topiramate & nalmefene conclusions for alcohol use outcomes

- Neither improve abstinence
- Fewer drinking days for Topiramate
- Fewer heavy drinking days for both
- Fewer drinks per drinking day for both
- Nalmefene not available here

= 2^{ND} LINE MEDICATION WITH MODERATE EVIDENCE—OFF LABEL FOR AUD

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Gabapentin conclusions for alcohol use outcomes

- May have efficacy for improved abstinence and reduced rate of return to heavy drinking\(^1\)
  - Small sample size

- Methodological problems with earlier favourable studies

= 2\(^{\text{ND}}\) LINE MEDICATION WITH LIMITED EVIDENCE —OFF LABEL FOR AUD

Baclofen conclusions for alcohol use outcomes

- Some evidence for improved abstinence, but small sample sizes\(^1,^2\)
- Possible early results for improved abstinence and consumption outcomes (at higher doses)\(^3\)

\(^3\) UpToDate. Pharmacotherapy for alcohol use disorder. 2015.
<table>
<thead>
<tr>
<th>Dose</th>
<th>CONTRAINDICATIONS</th>
<th>CONSIDERATIONS</th>
<th>Side Effects</th>
<th>Monitoring</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Naltrexone</strong></td>
<td>• Taking opioids, or anticipated to require</td>
<td>• Pregnancy: (risk category ‘C’) used more than others due to absence of known harms; but use cautiously due to absence of well-controlled studies for any of the med options in humans</td>
<td>• GI upset</td>
<td>• Liver enzymes at baseline, 1month, Q3/12</td>
</tr>
<tr>
<td></td>
<td>• Liver enzymes 3x normal</td>
<td></td>
<td></td>
<td>Discontinue if liver enzymes rise &gt;3x baseline</td>
</tr>
<tr>
<td></td>
<td>• Liver failure (caution with dysfunction or disease)</td>
<td></td>
<td>• Elevated liver enzymes</td>
<td></td>
</tr>
<tr>
<td>• 25mg x3d (to ➔ side effects), then ➔ to 50-100mg daily</td>
<td>• No need to abstain before starting po (depot not shown effective if drinking when started)</td>
<td></td>
<td></td>
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</tr>
<tr>
<td></td>
<td></td>
<td>• Glutupset</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Acamprosate</strong></td>
<td>• Serious renal disease</td>
<td>• Pregnancy: (risk category ‘C’), teratogenic in animals. No adequate studies</td>
<td>• GI upset</td>
<td>• Liver enzymes at baseline, 1month, Q3/12</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Cumbersome TID dosing</td>
<td></td>
<td>Discontinue if liver enzymes rise &gt;3x baseline</td>
</tr>
<tr>
<td>• 666mg TID; 333mg TID if renal impairment or &lt;60kg</td>
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<tr>
<td></td>
<td>Abstain for ≥ 4 days before initiation*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Disulfiram</strong></td>
<td>• End stage liver disease (e.g. cirrhosis)</td>
<td>• No risk category assigned as insufficient data to establish risk</td>
<td>• Initial—typically resolve within weeks:*</td>
<td>• Measure liver enzymes at baseline, 2 weeks, Q3/12</td>
</tr>
<tr>
<td></td>
<td>• Severe cardiovascular disease (e.g. CAD), Hx of CVA</td>
<td></td>
<td>• Fatigue</td>
<td>Discontinue if liver enzymes ≥3x normal</td>
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<tr>
<td></td>
<td>• Psychosis</td>
<td></td>
<td>• Headache</td>
<td></td>
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<tr>
<td></td>
<td>• Epileptic seizures</td>
<td></td>
<td>• Garlic-like taste &amp; smell</td>
<td></td>
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<tr>
<td></td>
<td>• Florid ulcers</td>
<td></td>
<td>• Hepatotoxicity (disulfiram-induced hepatitis)</td>
<td></td>
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<tr>
<td></td>
<td>• Rubber allergy</td>
<td></td>
<td>• Peripheral neuropathy</td>
<td></td>
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<tr>
<td></td>
<td>• Pregnancy</td>
<td></td>
<td>• Psychosis</td>
<td></td>
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<tr>
<td></td>
<td>• Cognitive impairment precluding understanding of disulfiram effect</td>
<td></td>
<td>• Depression</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• No risk category assigned as insufficient data to establish risk</td>
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<tr>
<td>• 250mg daily; Range 125-500mg</td>
<td>• End stage liver disease (e.g. cirrhosis)</td>
<td>• No risk category assigned as insufficient data to establish risk</td>
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</tr>
<tr>
<td>• Abstain for ≥ 2 days before initiation</td>
<td>• Glutupset</td>
<td>• Initial—typically resolve within weeks:3</td>
<td>• Measure liver enzymes at baseline, 2 weeks, Q3/12</td>
<td></td>
</tr>
<tr>
<td>• Disulfiram reaction can occur up to 14 days if they wish to resume ETOH</td>
<td>• Headache</td>
<td>• Fatigue</td>
<td>Discontinue if liver enzymes ≥3x normal</td>
<td></td>
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<td></td>
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<td>• Garlic-like taste &amp; smell</td>
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<td>• Depression</td>
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</tbody>
</table>

* Although acamprosate is only approved for use in established abstinence, studies support reduced heavy drinking for both naltrexone and acamprosate even if initiated while not yet abstinent.5

** Although not in current FDA labeling, SAMHSA consensus panel suggests avoiding if baseline aminotransferase levels >5x ULM “except where benefits outweigh the risks”.2

4 Uptodate. Pharmacotherapy in alcohol use disorder. 2015
Cost and availability

- Disulfiram not produced in Canada
  - May be accessed through compounding pharmacy
  - No coverage in any province or territory
  - Total cost for patient: $65/month, based on 100mg daily\(^1\)

\(^1\) Cost data provided by Pharmacist Rich Rego, Beacon Pharmacy, Calgary
## Cost and availability

### Naltrexone:
Available in Canada in 50mg scored po tablet

<table>
<thead>
<tr>
<th>No coverage:</th>
<th>AB, MB, SK, NL, NU, NT</th>
</tr>
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<tbody>
<tr>
<td>General benefit:</td>
<td>QC, YT</td>
</tr>
<tr>
<td>Special request process:</td>
<td>BC, ON, NB, NS, PE</td>
</tr>
</tbody>
</table>

- Covered by many private drug plans; if 70% covered, cost to patient: $65/month, based on 50mg daily\(^1\)
- **Not** currently a drug benefit under Social Services (AB)
- Cost to patient if no coverage: $215/month\(^1\)
- Depot available in US $?2000/mo

\(^1\) Cost data provided by Pharmacist Rich Rego, Beacon Pharmacy, Calgary
## Cost and availability

### Acamprosate:
Available in Canada in 333mg po tablet

<table>
<thead>
<tr>
<th>No coverage:</th>
<th>AB, MB, SK, YT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Special request process:</td>
<td>BC, ON, NB, NS, PE, NL, NT</td>
</tr>
<tr>
<td>NIHB:</td>
<td>NU</td>
</tr>
<tr>
<td>By eligibility criteria</td>
<td>QC</td>
</tr>
</tbody>
</table>

- Covered by many private drug plans; if 70% covered, cost to patient: $55/month, based on 333mg 2tabs tid\(^1\)
- **Not** currently a drug benefit under Social Services (AB)
- Cost to patient if no coverage: $184/month\(^1\)

\(^1\) Cost data provided by Pharmacist Rich Rego, Beacon Pharmacy, Calgary
Topiramate

- Dose: Generally initiated at 50mg daily titrated gradually over several weeks to 150mg BID
  - Adverse events include cognitive impairment (word naming difficulties), paresthesias, weight loss, headache, fatigue dizziness, depression\(^1\)
  - Slow titration can mitigate side effects

- The only medication for AUD requiring taper to discontinue

- Pregnancy risk category “D” increased risk of cleft lip and or palate, although occurrence rare\(^1\)

- Off-label

- Drug benefit under Social Services (AB)

- Covered by many private drug plans; if 80% covered, cost to patient: $15/month, based on 150mg BID

- Cost to patient if no coverage: $75/month\(^2\)

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\(^1\) Uptodate. Pharmacotherapy for alcohol use disorder. 2015
\(^2\) Cost data provided by Pharmacist Rich Rego, Beacon Pharmacy, Calgary
Gabapentin

- Off-label
- Drug benefit under Social Services (AB)
- Dose: 300mg TID?, 600mg TID?
  - Well-tolerated at lower doses¹
  - Higher: sedation, dizziness¹
- Covered by many private drug plans; if 80% covered, cost to patient: $6/month, based on 300mg tid²
- Cost to patient if no coverage: $30/month²
- Some concern about abuse potential³,⁴,⁵,⁶

¹ Uptodate. Pharmacotherapy for alcohol use disorder. 2015
² Cost data provided by Pharmacist Rich Rego, Beacon Pharmacy, Calgary
Baclofen

- Off-label

- Drug benefit under Social Services (AB)

- Dose: 30mg daily, 60mg daily?
  - Well tolerated with no serious adverse events
  - Occurred > placebo: nausea, vertigo, transient sleepiness, abdo pain

- Covered by many private drug plans; if 80% covered, cost to patient: $6/month, based on 60mg daily

- Drug benefit under Social Services (AB)

- Cost to patient if no coverage: $28/month

- Appears safe in severe hepatic disease

- No abuse liability

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1 Uptodate. Pharmacotherapy for alcohol use disorder. 2015
2 Cost data provided by Pharmacist Rich Rego, Beacon Pharmacy, Calgary
Case #1

- **ID:** 32 year old pregnant, 1st trimester
- **Chief Concern:** A friend told her about success quitting ETOH using medication. Wants to try Rx.
- **HPI:** 13oz daily. Past Sobriety only while on acamprosate. Multiple failed attempts at abstinence with residential tx alone. No other medications tried.
- **PMHx:** Multiple admissions for alcohol related injuries and severe withdrawal.
- **Meds/allergies:** PN vit. daily, good compliance; NKDA
- **Social:** Lives with husband and their 4 year old daughter; employed at book store with Blue Cross coverage

WHAT WOULD YOU ADVISE RE: PHARMACOTHERAPY?
Answer—Case #1

- Naltrexone could be considered if benefits thought to outweigh risks

- Pregnancy risk category ‘C’, Risk cannot be ruled out:
  - Naltrexone, Acamprosate, Gabapentin, Baclofen

- Pregnancy risk category ‘D’, Positive evidence of risk:
  - Topiramate (cleft lip and/or cleft palate, although rare)

- No risk category assigned as insufficient data to establish risk
  - Disulfiram (rarely used in pregnancy)

No safe pharmacotherapy options in pregnancy—consider if benefits outweigh risks

How might advice differ if patient on social assistance?
Case #2

- ID: 34 year old female
- Chief Concern: Request medication for AUD
- HPI: Diagnosed 3 years ago with AUD severe; multiple failed residential treatment attempts at abstinence
- PMHx: Crohn’s Disease with occasional flares requiring hospitalization ~once yearly
- Meds/allergies: none currently/none
- Social: FT Teacher; Single never married; Blue Cross Medication coverage through work;
Case #2

- Which of the following would **not** be a suitable option?
  - Naltrexone
  - Acamprosate
  - Disulfiram
  - Topiramate
  - Gabapentin
  - Baclofen
Answer—Case #2

- Crohn’s flare may require opioids to control pain
- Naltrexone contraindicated in individuals taking/anticipated to require opioids
Case #3

- ID: 57 year old male, AUD-moderate
- Chief Concern: Wants help to quit drinking; Interested in outpatient tx, but open to considering medication as well
- HPI: Detoxed in hospital after falling and breaking leg while intoxicated; drinking most days each week since age 18; several 2-8 year periods of abstinence; last abstinent x 4yrs ending in 2013
- PMHx: DM2, HTN,
- Meds: Metformin BID (difficulty remembering to take suppertime dose); Ramipril once daily; Crestor daily; ASA
- Social: On short-term disability while leg fracture heals; wants to keep working as electrician until age 65, so he can collect pension; Has drug coverage through work
Case #3

Which of the following two would **not** be good options?

- Naltrexone
- Acamprosate
- Disulfiram
- Topiramate
- Gabapentin
- Baclofen
Answer—Case #3

- Given his difficulty remembering to take multiple daily doses of metformin, acamprosate with TID dosing may NOT be a good option; likewise topiramate and gabapentin are BID and TID respectively

- Topiramate may not be a good option as can cause cognitive impairment
Case #4

- **ID:** 30 year old male, AUD-moderate-severe
- **Chief Concern:** Wants medication to augment residential treatment
- **HPI:** Detoxed x 5 days; on his way to 3 week residential tx program; no contraindications to any med option
- **PMHx:** Otherwise well
- **Meds/allergies:** None/none
- **Social:** On Social Assistance

**WHAT WOULD YOU ADVISE RE: PHARMACOTHERAPY?**
Answer—Case #4

- Social Assistance (in AB) does not cover Naltrexone, Acamprosate (best evidence), Disulfiram (limited evidence)

- Might consider off-label use of Topiramate (moderate evidence), followed by Gabapentin, Baclofen (limited evidence)

- Thorough discussion re: *may* be effective but safety and effectiveness data for this indication lacking; Is risk of taking despite lack of proven benefits worth potential benefit?
Case #5

- **ID:** 30 year old male, AUD—severe
- **Chief Concern:** Wants medication to augment residential treatment
- **HPI:** Just out of hospital after admission for decompensated alcoholic cirrhosis; wants to attend residential and remain sober in order to become candidate for liver transplant; liver enzymes elevated >7x upper limit of normal
- **PMHx:** Well aside from chronic severe liver disease
- **Social:** Rented apartment funded by large inheritance

**WHAT WOULD YOU ADVISE RE: PHARMACOTHERAPY?**

**HOW MIGHT ADVICE DIFFER IF PATIENT ON SOCIAL ASSISTANCE?**
Answer—Case #5

- Naltrexone and disulfiram contraindicated in severe liver disease

- Acamprosate can be used in severe liver disease (but not renal); (best evidence)

- Baclofen? There is *some* evidence for the use of baclofen, which appears to be safe in severe hepatic disease.
  - Off label use
  - Is covered by AB Works
Case #6

- Patient wants to go on medication for severe AUD and is good candidate, has funding in place for all options.
- Has severe liver disease
- Is unable to stop drinking for more than a few hours; does not want to attend detox

WHAT MIGHT YOU ADVISE FOR PHARMACOTHERAPY?
Case #6

- No need to abstain prior to starting naltrexone; but contraindicated in severe liver disease

- Disulfiram requires abstinence x 2 days prior to initiation and is contraindicated in severe liver disease

- Abstinence suggested prior to initiating acamprosate, however, as noted above, some evidence for reduction in ETOH use even if drinking at initiation