Pharmacotherapy Options for Alcohol Use Disorder

<table>
<thead>
<tr>
<th>Contraindications</th>
<th>Naltrexone</th>
<th>Acamprosate</th>
<th>Topiramate</th>
<th>Gabapentin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Concurrent Alcohol Use</td>
<td>No well-described safety risk</td>
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</tr>
<tr>
<td></td>
<td>Tx after WDM may be more effective</td>
<td>Tx after WDM may be more effective</td>
<td></td>
<td>Abstinence for ≥3 days may improve outcomes</td>
</tr>
<tr>
<td></td>
<td>1. Naltrexone hypersensitivity</td>
<td>1. Acamprosate hypersensitivity</td>
<td>1. Topiramate hypersensitivity</td>
<td>Gabapentin hypersensitivity</td>
</tr>
<tr>
<td></td>
<td>2. Any current opioid use (Rx or nonmedical)</td>
<td>2. Severe renal impairment</td>
<td>2. Pregnant or planning pregnancy</td>
<td></td>
</tr>
<tr>
<td></td>
<td>4. Acute hepatitis or liver failure</td>
<td></td>
<td>4. Nephrolithiasis</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Cautions</th>
<th>Naltrexone</th>
<th>Acamprosate</th>
<th>Topiramate</th>
<th>Gabapentin</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Renal impairment</td>
<td></td>
<td></td>
<td>1. Concomitant use of valproic acid</td>
<td>1. Renal impairment</td>
</tr>
<tr>
<td>2. Severe hepatic impairment</td>
<td></td>
<td></td>
<td>2. Conditions/therapies that predispose to acidosis</td>
<td>2. Pregnancy and breastfeeding*</td>
</tr>
<tr>
<td>3. Concomitant use of other potentially hepatotoxic drugs</td>
<td></td>
<td></td>
<td>3. Adolescent and geriatric (&gt;65 years) patients*</td>
<td>3. Adolescent and geriatric (&gt;65 years) patients*</td>
</tr>
<tr>
<td>5. Adolescent patients (&lt;18 years)*</td>
<td></td>
<td></td>
<td>5. Compromised respiratory function</td>
<td>5. Compromised respiratory function</td>
</tr>
<tr>
<td></td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Side Effects</th>
<th>Nausea, headache, and dizziness</th>
<th>Diarrhea, vomiting, and abdominal pain</th>
<th>Psychomotor slowing, difficulty concentrating, speech/language problems, somnolence, fatigue, and mood disturbance</th>
<th>Ataxia, slurred speech, and drowsiness</th>
</tr>
</thead>
<tbody>
<tr>
<td>Starting at low dose and/or abstinence can reduce side effects</td>
<td></td>
<td></td>
<td>Starting at low dose and titrating up can reduce side effects</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Coverage and Cost**</th>
<th>Full coverage under Fair PharmaCare, and PharmaCare Plans C, G, and W</th>
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</tr>
</thead>
<tbody>
<tr>
<td>$105 per month</td>
<td>$165 per month</td>
<td>$75 per month</td>
</tr>
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<tr>
<th>Safety and Other Considerations</th>
<th>Naltrexone</th>
<th>Acamprosate</th>
<th>Topiramate</th>
<th>Gabapentin</th>
</tr>
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<tr>
<td>Liver function tests (LFT) at initial tx, and 1, 3, and 6 mo. More frequent monitoring if LFTs are elevated</td>
<td>No safety risk w/ mild renal impairment</td>
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<td>Due to risk of fetal harm, advise women to use effective contraception</td>
<td>No safety risk w/ liver disease</td>
</tr>
<tr>
<td>Due to risk of hepatic injury, advise patients on signs of acute hepatitis and to stop tx if symptoms appear</td>
<td>Moderate impairment requires dose reduction</td>
<td>No hepatic toxicity</td>
<td>Monitor for signs of hyperammonemia and metabolic acidosis</td>
<td>Requires conservative dosing in patients with renal impairment</td>
</tr>
</tbody>
</table>

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<tr>
<th>Dosing</th>
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<th>Topiramate</th>
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<tbody>
<tr>
<td>Start: 12.5mg BID for 3 days</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Titrate: to 50mg OD over 2 wks as tolerated</td>
<td>2 x 333mg tablets TID</td>
<td></td>
<td>Titrate: to 2 x 50mg tablets BID over several wks as tolerated</td>
<td>Start: at 100-300mg TID, Titrate: PRN to 1800mg max daily</td>
</tr>
</tbody>
</table>

**Safety and efficacy has not been well established in these patient populations. Careful assessment of benefit and risks, fully informed patient consent, and more frequent monitoring is advised.**

**Estimated cost if patient is not eligible for coverage**

Abbreviations: WDM – withdrawal management, PRN – as needed/when necessary, TID – three times per day, BID – two times per day, OD – once daily
## Pharmacotherapy Options for Outpatient Management of Alcohol Withdrawal

### Concurrent Alcohol Use
- Potentiates effects of alcohol; can lead to serious safety risks, incl. over sedation, falls, delirium, respiratory depression (e.g., non-fatal or fatal overdose), and prolonged hospitalization

### Contraindications
1. Severe respiratory insufficiency
2. Hepatic disease
3. Sleep apnea
4. Myasthenia gravis
5. Narrow angle glaucoma

### Cautions
1. Lactose intolerance
2. Renal impairment
3. Breastfeeding

### Side Effects
- Drowsiness, dizziness
- Less common: changes in skin colour, nausea, headache, blurred vision, tremors, hypotension, GI disturbances, memory loss

### Other Considerations
- Potential for non-medical use, diversion, and dependence
- Potential for drug-drug interactions leading to excess sedation, impaired psychomotor and cognitive functioning.
- Due to safety concerns, exercise caution with outpatient use
- Lorazepam is preferred for those with severe respiratory or liver disease and in elderly (consider lower dosing)

### Dosing
- **Diazepam (Valium)**
  - **Day 1**: 10mg QID
  - **Day 2**: 10mg TID
  - **Day 3**: 10mg BID
  - **Day 4**: 10mg HS
- **Lorazepam (Ativan)**
  - **Day 1-2**: 2mg every 4h
  - **Day 3-4**: 1mg every 4h

### Benzodiazepines

### Carbamazepine
- No well-described safety risk
- Abstinence recommended after tx due to risk of additive CNS-depressive effects
  - **Note**: Studies suggest at therapeutic doses gabapentin is not likely to increase sedation or motor impairment

### Gabapentin
- Hypersensitivity to gabapentin

### Clonidine
- Risk of additive effect on lowering BP

### Benzodiazepines
- Lorazepam is preferred for those with severe respiratory or liver disease and in elderly (consider lower dosing)

### Carbamazepine
- **Contraindications**
  - Severe respiratory insufficiency
  - Hepatic disease
  - Bone marrow depression
  - Myasthenia gravis
  - Narrow angle glaucoma

### Gabapentin
- **Contraindications**
  - Sinus node function impairment
  - Severe bradyarrhythmia
  - Galactose intolerance
- **Cautions**
  - Lactose intolerance
  - Renal impairment
  - Breastfeeding

### Clonidine
- **Contraindications**
  - Hepatic disease
  - Bone marrow depression
  - Serious blood disorder
  - Atrioventricular heart block
- **Hypersensitivity**
  - Sinus node function impairment
  - Severe bradyarrhythmia
  - Galactose intolerance
- **Side Effects**
  - Drowsiness, dizziness
  - Less common: changes in skin colour, nausea, headache, blurred vision, tremors, hypotension, GI disturbances, memory loss

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  - **Day 3-4**: 1mg every 4h

### Notes
- All medications are eligible for full coverage under Fair PharmaCare, and PharmaCare Plans C and W.
- **Abbreviations**: BP – blood pressure, PRN – as needed/when necessary, QID – four times per day, TID – three times per day, BID – two times per day, OD – once daily, HS – at bedtime
- *Due to higher prevalence of the HLA-B*1502 allele. Genetic testing must be performed to exclude those at high-risk

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**BRITISH COLUMBIA CENTRE ON SUBSTANCE USE**