

## Pharmacotherapy Options for Alcohol Use Disorder

|  | <i>First Line Pharmacotherapy</i>   |   | <i>Second Line Pharmacotherapy</i>  |   |
|--|---|---|---|---|
|  | <b>Naltrexone</b>   | <b>Acamprosate</b>  | <b>Topiramate</b>   | <b>Gabapentin</b>   |
| <b>Concurrent Alcohol Use</b>          | No well-described safety risk<br>Tx after WDM may be more effective   | No well-described safety risk<br>Tx after WDM may be more effective   | No well-described safety risk   | No well-described safety risk at therapeutic dose<br>Abstinence recommended after tx<br>Abstinence for ≥3 days may improve outcomes   |
| <b>Contra-indications</b>              | <ol style="list-style-type: none"> <li>1. Naltrexone hypersensitivity</li> <li>2. Any current opioid use (Rx or nonmedical)</li> <li>3. Acute opioid withdrawal</li> <li>4. Acute hepatitis or liver failure</li> </ol>   | <ol style="list-style-type: none"> <li>1. Acamprosate hypersensitivity</li> <li>2. Severe renal impairment</li> <li>3. Breastfeeding</li> </ol>                     | <ol style="list-style-type: none"> <li>1. Topiramate hypersensitivity</li> <li>2. Pregnant or planning pregnancy</li> <li>3. Narrow angle glaucoma</li> <li>4. Nephrolithiasis</li> </ol> | Gabapentin hypersensitivity   |
| <b>Cautions</b>                        | <ol style="list-style-type: none"> <li>1. Renal impairment</li> <li>2. Severe hepatic impairment</li> <li>3. Concomitant use of other potentially hepatotoxic drugs</li> <li>4. Pregnancy and breastfeeding*</li> <li>5. Adolescent patients (&lt;18 years)*</li> </ol> | <ol style="list-style-type: none"> <li>1. Moderate renal impairment</li> <li>2. Adolescent and geriatric (&gt;65 years) patients*</li> <li>3. Pregnancy*</li> </ol> | <ol style="list-style-type: none"> <li>1. Concomitant use of valproic acid</li> <li>2. Conditions/therapies that predispose to acidosis</li> </ol>  | <ol style="list-style-type: none"> <li>1. Renal impairment</li> <li>2. Pregnancy and breastfeeding*</li> <li>3. Adolescent and geriatric (&gt;65 years) patients*</li> <li>4. Concomitant use of opioids and other CNS depressants</li> <li>5. Compromised respiratory function</li> <li>6. Neurological disease or cognitive impairment</li> </ol> |
| <b>Side Effects</b>                    | Nausea, headache, and dizziness<br>Starting at low dose and/or abstinence can reduce side effects   | Diarrhea, vomiting, and abdominal pain  | Psychomotor slowing, difficulty concentrating, speech/language problems, somnolence, fatigue, and mood disturbance<br>Starting at low dose and titrating up can reduce side effects       | Ataxia, slurred speech, and drowsiness  |
| <b>Coverage and Cost**</b>             | Full coverage under Fair PharmaCare, and PharmaCare Plans C, G, and W<br>Requires the Collaborative Prescribing Agreement   |   | Full coverage under Fair PharmaCare, and PharmaCare Plans C and W   |   |
|  | \$105 per month   | \$165 per month   | \$75 per month  | \$30 per month  |
| <b>Safety and Other Considerations</b> | Liver function tests (LFT) at initial tx, and 1, 3, and 6 mo. More frequent monitoring if LFTs are elevated<br><br>Due to risk of hepatic injury, advise patients on signs of acute hepatitis and to stop tx if symptoms appear   | No safety risk w/ mild renal impairment<br>Moderate impairment requires dose reduction<br><br>No hepatic toxicity   | Due to risk of fetal harm, advise women to use effective contraception<br>No safety risk w/ liver disease<br>Monitor for signs of hyperammonemia and metabolic acidosis                   | No safety risk w/ liver disease<br>Requires conservative dosing in patients with renal impairment   |
| <b>Dosing</b>                          | <b>Start:</b> 12.5mg BID for 3 days<br><b>Titrate:</b> to 50mg OD over 2 wks as tolerated   | 2 x 333mg tablets TID   | <b>Titrate:</b> to 2 x 50mg tablets BID over several wks as tolerated   | <b>Start:</b> at 100-300mg TID,<br><b>Titrate:</b> PRN to 1800mg max daily  |

# Pharmacotherapy Options for Outpatient Management of Alcohol Withdrawal

|  | Benzodiazepines  | Carbamazepine  | Gabapentin   | Clonidine   |          |       |          |       |         |         |              |         |              |  |       |                      |       |                         |       |           |         |          |   |       |  |                                      |  |           |  |   |  |                            |  |                                   |  |                             |  |  |  |  |       |                              |         |                               |            |                     |
|--|--|--|--|---|----------|-------|----------|-------|---------|---------|--------------|---------|--------------|--|-------|----------------------|-------|-------------------------|-------|-----------|---------|----------|---|-------|--|--------------------------------------|--|-----------|--|---|--|----------------------------|--|-----------------------------------|--|-----------------------------|--|--|--|--|-------|------------------------------|---------|-------------------------------|------------|---------------------|
| <b>Concurrent Alcohol Use</b>                              | 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  | No well-described safety risk  | Abstinence recommended after tx due to risk of additive CNS-depressive effects<br><i>Note:</i> Studies suggest at therapeutic doses gabapentin is <b>not</b> likely to increase sedation or motor impairment | Risk of additive effect on lowering BP  |          |       |          |       |         |         |              |         |              |  |       |                      |       |                         |       |           |         |          |   |       |  |                                      |  |           |  |   |  |                            |  |                                   |  |                             |  |  |  |  |       |                              |         |                               |            |                     |
| <b>Contra-indications</b>                                  | <ol style="list-style-type: none"> <li>Severe respiratory insufficiency</li> <li>Hepatic disease</li> <li>Sleep apnea</li> <li>Myasthenia gravis</li> <li>Narrow angle glaucoma</li> </ol>   | <ol style="list-style-type: none"> <li>Hepatic disease</li> <li>Bone marrow depression</li> <li>Serious blood disorder</li> <li>Atrioventricular heart block</li> </ol>  | Hypersensitivity to gabapentin   | <ol style="list-style-type: none"> <li>Sinus node function impairment</li> <li>Severe bradyarrhythmia</li> <li>Galactose intolerance</li> </ol>   |          |       |          |       |         |         |              |         |              |  |       |                      |       |                         |       |           |         |          |   |       |  |                                      |  |           |  |   |  |                            |  |                                   |  |                             |  |  |  |  |       |                              |         |                               |            |                     |
| <b>Cautions</b>  | <ol style="list-style-type: none"> <li>Lactose intolerance</li> <li>Renal impairment</li> <li>Breastfeeding</li> </ol>   | Associated with rare blood dyscrasias and Stevens Johnson Syndrome with long-term use<br><br>*Asian ethnicity increases risk of carbamazepine toxicity   | Renal impairment   | Hypotension in sensitive patients   |          |       |          |       |         |         |              |         |              |  |       |                      |       |                         |       |           |         |          |   |       |  |                                      |  |           |  |   |  |                            |  |                                   |  |                             |  |  |  |  |       |                              |         |                               |            |                     |
| <b>Side Effects</b>  | Drowsiness, dizziness<br>Less common: changes in skin colour, nausea, headache, blurred vision, tremors, hypotension, GI disturbances, memory loss   | Dizziness, pruritus, ataxia, headache, drowsiness and nausea (all usually minor and temporary)   | Higher doses may cause ataxia, slurred speech and/or drowsiness<br>Profile is better than other anticonvulsants.   | Hypotension, dry mouth, dizziness, fatigue, headache, nausea, vomiting, constipation, malaise, sleep disorder, sedation and erectile dysfunction  |          |       |          |       |         |         |              |         |              |  |       |                      |       |                         |       |           |         |          |   |       |  |                                      |  |           |  |   |  |                            |  |                                   |  |                             |  |  |  |  |       |                              |         |                               |            |                     |
| <b>Other Considerations</b>                                | Potential for non-medical use, diversion, and dependence<br><br>Potential for drug-drug interactions leading to excess sedation, impaired psychomotor and cognitive functioning.<br><br>Due to safety concerns, exercise caution with outpatient use<br><br>Lorazepam is preferred for those with severe respiratory or liver disease and in elderly (consider lower dosing) | No risk of non-medical use, diversion, or dependence<br><br>Some side effects resemble w/drawal symptoms; confirm source of symptoms before dose adjustments<br><br>Baseline and periodic evaluations of hepatic function must be performed in elderly patients and patients w/ history of liver disease | Potential for non-medical use, diversion, and dependence<br><br>Toxicity profile parallels that of alcohol.<br><br>Easy to transition from WDM to long-term relapse prevention.                              | Only use for mild-moderate w/drawal symptoms when low risk of severe complications<br><br>Safe as adjunct to benzodiazepines or other anticonvulsants<br><br>Provide education on the signs and symptoms of hypotension |          |       |          |       |         |         |              |         |              |  |       |                      |       |                         |       |           |         |          |   |       |  |                                      |  |           |  |   |  |                            |  |                                   |  |                             |  |  |  |  |       |                              |         |                               |            |                     |
| <b>Dosing</b>  | Diazepam (Valium)<br><table border="1"> <tr><td>Day 1</td><td>10mg QID</td></tr> <tr><td>Day 2</td><td>10mg TID</td></tr> <tr><td>Day 3</td><td>10mg BID</td></tr> <tr><td>Day 4</td><td>10mg HS</td></tr> </table><br>Lorazepam (Ativan)<br><table border="1"> <tr><td>Day 1-2</td><td>2mg every 4h</td></tr> <tr><td>Day 3-4</td><td>1mg every 4h</td></tr> </table>       | Day 1  | 10mg QID   | Day 2   | 10mg TID | Day 3 | 10mg BID | Day 4 | 10mg HS | Day 1-2 | 2mg every 4h | Day 3-4 | 1mg every 4h | For immediate-release tablets<br><table border="1"> <tr><td>Day 1</td><td>Start with 200mg QID</td></tr> <tr><td>Day 2</td><td>Taper down to 200mg TID</td></tr> <tr><td>Day 3</td><td>200mg BID</td></tr> <tr><td>Day 4-5</td><td>200mg HS</td></tr> </table> | Day 1 | Start with 200mg QID | Day 2 | Taper down to 200mg TID | Day 3 | 200mg BID | Day 4-5 | 200mg HS | For immediate-release tablets<br><table border="1"> <tr><td colspan="2">Start</td></tr> <tr><td colspan="2">300mg TID + 300mg PRN +600-1200mg HS</td></tr> <tr><td colspan="2">Titration</td></tr> <tr><td colspan="2">Quickly to 600mg TID + 600-1200mg HS as tolerated</td></tr> <tr><td colspan="2">Do not exceed 3600mg daily</td></tr> <tr><td colspan="2">Taper when acute symptoms resolve</td></tr> <tr><td colspan="2">To 600mg TID + 600-900mg HS</td></tr> <tr><td colspan="2">To zero over next 3-5 days, decreasing dose by 600mg daily</td></tr> </table> | Start |  | 300mg TID + 300mg PRN +600-1200mg HS |  | Titration |  | Quickly to 600mg TID + 600-1200mg HS as tolerated |  | Do not exceed 3600mg daily |  | Taper when acute symptoms resolve |  | To 600mg TID + 600-900mg HS |  | To zero over next 3-5 days, decreasing dose by 600mg daily |  | Typically an adjunct tx<br><table border="1"> <tr><td>Start</td><td>0.1-0.2mg BID (last dose HS)</td></tr> <tr><td>Titrate</td><td>Can add 0.2mg daily if needed</td></tr> <tr><td>Final dose</td><td>Range 0.1-0.6mg BID</td></tr> </table> | Start | 0.1-0.2mg BID (last dose HS) | Titrate | Can add 0.2mg daily if needed | Final dose | Range 0.1-0.6mg BID |
| Day 1  | 10mg QID   |  |  |   |          |       |          |       |         |         |              |         |              |  |       |                      |       |                         |       |           |         |          |   |       |  |                                      |  |           |  |   |  |                            |  |                                   |  |                             |  |  |  |  |       |                              |         |                               |            |                     |
| Day 2  | 10mg TID   |  |  |   |          |       |          |       |         |         |              |         |              |  |       |                      |       |                         |       |           |         |          |   |       |  |                                      |  |           |  |   |  |                            |  |                                   |  |                             |  |  |  |  |       |                              |         |                               |            |                     |
| Day 3  | 10mg BID   |  |  |   |          |       |          |       |         |         |              |         |              |  |       |                      |       |                         |       |           |         |          |   |       |  |                                      |  |           |  |   |  |                            |  |                                   |  |                             |  |  |  |  |       |                              |         |                               |            |                     |
| Day 4  | 10mg HS  |  |  |   |          |       |          |       |         |         |              |         |              |  |       |                      |       |                         |       |           |         |          |   |       |  |                                      |  |           |  |   |  |                            |  |                                   |  |                             |  |  |  |  |       |                              |         |                               |            |                     |
| Day 1-2  | 2mg every 4h   |  |  |   |          |       |          |       |         |         |              |         |              |  |       |                      |       |                         |       |           |         |          |   |       |  |                                      |  |           |  |   |  |                            |  |                                   |  |                             |  |  |  |  |       |                              |         |                               |            |                     |
| Day 3-4  | 1mg every 4h   |  |  |   |          |       |          |       |         |         |              |         |              |  |       |                      |       |                         |       |           |         |          |   |       |  |                                      |  |           |  |   |  |                            |  |                                   |  |                             |  |  |  |  |       |                              |         |                               |            |                     |
| Day 1  | Start with 200mg QID   |  |  |   |          |       |          |       |         |         |              |         |              |  |       |                      |       |                         |       |           |         |          |   |       |  |                                      |  |           |  |   |  |                            |  |                                   |  |                             |  |  |  |  |       |                              |         |                               |            |                     |
| Day 2  | Taper down to 200mg TID  |  |  |   |          |       |          |       |         |         |              |         |              |  |       |                      |       |                         |       |           |         |          |   |       |  |                                      |  |           |  |   |  |                            |  |                                   |  |                             |  |  |  |  |       |                              |         |                               |            |                     |
| Day 3  | 200mg BID  |  |  |   |          |       |          |       |         |         |              |         |              |  |       |                      |       |                         |       |           |         |          |   |       |  |                                      |  |           |  |   |  |                            |  |                                   |  |                             |  |  |  |  |       |                              |         |                               |            |                     |
| Day 4-5  | 200mg HS   |  |  |   |          |       |          |       |         |         |              |         |              |  |       |                      |       |                         |       |           |         |          |   |       |  |                                      |  |           |  |   |  |                            |  |                                   |  |                             |  |  |  |  |       |                              |         |                               |            |                     |
| Start  |  |  |  |   |          |       |          |       |         |         |              |         |              |  |       |                      |       |                         |       |           |         |          |   |       |  |                                      |  |           |  |   |  |                            |  |                                   |  |                             |  |  |  |  |       |                              |         |                               |            |                     |
| 300mg TID + 300mg PRN +600-1200mg HS                       |  |  |  |   |          |       |          |       |         |         |              |         |              |  |       |                      |       |                         |       |           |         |          |   |       |  |                                      |  |           |  |   |  |                            |  |                                   |  |                             |  |  |  |  |       |                              |         |                               |            |                     |
| Titration  |  |  |  |   |          |       |          |       |         |         |              |         |              |  |       |                      |       |                         |       |           |         |          |   |       |  |                                      |  |           |  |   |  |                            |  |                                   |  |                             |  |  |  |  |       |                              |         |                               |            |                     |
| Quickly to 600mg TID + 600-1200mg HS as tolerated          |  |  |  |   |          |       |          |       |         |         |              |         |              |  |       |                      |       |                         |       |           |         |          |   |       |  |                                      |  |           |  |   |  |                            |  |                                   |  |                             |  |  |  |  |       |                              |         |                               |            |                     |
| Do not exceed 3600mg daily                                 |  |  |  |   |          |       |          |       |         |         |              |         |              |  |       |                      |       |                         |       |           |         |          |   |       |  |                                      |  |           |  |   |  |                            |  |                                   |  |                             |  |  |  |  |       |                              |         |                               |            |                     |
| Taper when acute symptoms resolve                          |  |  |  |   |          |       |          |       |         |         |              |         |              |  |       |                      |       |                         |       |           |         |          |   |       |  |                                      |  |           |  |   |  |                            |  |                                   |  |                             |  |  |  |  |       |                              |         |                               |            |                     |
| To 600mg TID + 600-900mg HS                                |  |  |  |   |          |       |          |       |         |         |              |         |              |  |       |                      |       |                         |       |           |         |          |   |       |  |                                      |  |           |  |   |  |                            |  |                                   |  |                             |  |  |  |  |       |                              |         |                               |            |                     |
| To zero over next 3-5 days, decreasing dose by 600mg daily |  |  |  |   |          |       |          |       |         |         |              |         |              |  |       |                      |       |                         |       |           |         |          |   |       |  |                                      |  |           |  |   |  |                            |  |                                   |  |                             |  |  |  |  |       |                              |         |                               |            |                     |
| Start  | 0.1-0.2mg BID (last dose HS)   |  |  |   |          |       |          |       |         |         |              |         |              |  |       |                      |       |                         |       |           |         |          |   |       |  |                                      |  |           |  |   |  |                            |  |                                   |  |                             |  |  |  |  |       |                              |         |                               |            |                     |
| Titrate  | Can add 0.2mg daily if needed  |  |  |   |          |       |          |       |         |         |              |         |              |  |       |                      |       |                         |       |           |         |          |   |       |  |                                      |  |           |  |   |  |                            |  |                                   |  |                             |  |  |  |  |       |                              |         |                               |            |                     |
| Final dose   | Range 0.1-0.6mg BID  |  |  |   |          |       |          |       |         |         |              |         |              |  |       |                      |       |                         |       |           |         |          |   |       |  |                                      |  |           |  |   |  |                            |  |                                   |  |                             |  |  |  |  |       |                              |         |                               |            |                     |