

**U.S. Department of Veterans Affairs** 

Veterans Health Administration PBM Academic Detailing Services A QUICK REFERENCE GUIDE (2022)

# **Alcohol Use Disorder (AUD)**

## Leading the Charge in the Treatment of AUD

## VA PBM Academic Detailing Services Real Provider Resources Real Patient Results

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## **AUD: Cutoffs for Concern**

Patients who drink above the recommended limits account for most of the morbidity and mortality attributed to AUD.<sup>1,2</sup>

## **Drinking Levels<sup>3</sup>**

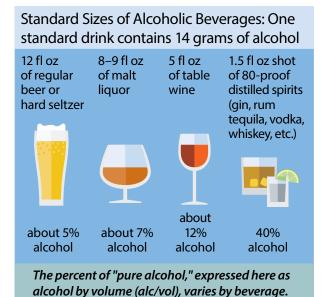
Gender	Drinking in Moderation	Binge Drinking*	Heavy/Excessive Alcohol use
Males	0 – 2 drinks per day	≥5 drinks at the same time or within a couple of hours of each other	>4 drinks on any day <b>or</b> >14 drinks per week
Females and/or Age >65	0 – 1 drink per day	≥4 drinks at the same time or within a couple of hours of each other	>3 drinks on any day <b>or</b> >7 drinks per week

\*In the past month.

Older adults and women have increased sensitivity to alcohol because they typically metabolize it at a slower rate. This makes them more susceptible to the adverse consequences associated with alcohol consumption.

### How Many Drinks Are in Common Containers?

Regular Beer (5% alc/vol)	Malt Liquor (7% alc/vol)	Table Wine (12% alc/vol)	80-proof Distilled Spirits (40% alc/vol)
12 fl oz = 1	12 fl oz = $1\frac{1}{2}$	Regular wine bottle	A shot (1.5-oz glass/50ml
$16 \text{ fl oz} = 1\frac{1}{2}$	16 fl oz = 2	750 ml = 5	bottle) = 1
22 fl oz = 2	22 fl oz = $2\frac{1}{2}$		200 ml (a "half pint") = 4½
40 fl oz = 3½	40 fl oz = 4½		375 ml (a "pint" or "half bottle") = 8½ 750 ml (a "fifth") = 17



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## Screening — Alcohol Use Disorders Identification Test (AUDIT-C)<sup>4</sup>

Question	0 Points	1 Point	2 Points	3 Points	4 Points
How often did you have a drink containing alcohol in the past year?	Never	Monthly or less	2–4 times per month	2–3 times per week	4 or more times per week
On days in the past year when you drank alcohol, how many drinks did you typically drink?	1–2	3-4	5–6	7–9	10 or more
Female: How often did you have 4 or more drinks on one occasion in the past year?	Never	Less than monthly	Monthly	Weekly	Daily or almost daily
<b>Male:</b> How often did you have 6 or more drinks on one occasion in the past year?					

To better account for safer drinking levels in females, AUDIT-C item three is automatically tailored to the sex assigned at birth in the clinical reminder. For VA, an AUDIT-C score of 5 or more is considered positive for both men and women, and documentation of brief alcohol counseling is required.

## Spectrum of Unhealthy Alcohol Use with AUDIT-C Score and Recommended Treatment



A brief overview of recommended treatments by AUDIT-C score from low to high risk:

- Patients who practice abstinence or present a low-risk of drinking, AUDIT-C of 0 to 3, are recommended health promotion.
- Patients with a moderate-risk of drinking, AUDIT-C of 4 to 5, are recommended brief intervention.
- Patients at high-risk of drinking, AUDIT-C of 6 to 7, are recommended to brief interventions with or without pharmacotherapy and psychosocial interventions.
- Patients at severe-risk of drinking fall into two AUDIT C ranges: 8 to 9 and 10 to 12. Patients with an AUDIT-C range of 8 to 9 are recommended pharmacotherapy with or without psychosocial interventions and specialty care management. Lastly, patients in the highest AUDIT-C range of 10 to 12 are recommended specialty care management.

## Laboratory Monitoring of Alcohol Biomarkers

How Can They Be Used?<sup>19-23, 25</sup>

Screening tool

- Measuring biomarkers may assist in differential diagnosis.
- Positive predictive value increases when ≥2 indirect biomarkers are elevated.<sup>24</sup>

Motivating change in drinking behavior

Biomarker measurement can help motivate changes in drinking behaviors.

Identifying relapse to drinking

- For example, relapse to alcohol use after abstinence may be best identified by a simultaneous 30% increase in Carbohydrate-Deficient Transferrin (CDT) and Gamma-glutamyl transferase (GGT) elevation.
- Addressing relapse early can prevent further alcohol misuse.

## Laboratory Monitoring for Alcohol Use Disorders

### Indirect Biomarkers<sup>19–23,25</sup>

Biomarker (elevated)	Type of Drinking Characterized	Time to Return to Normal with Abstinence	Possible Source of False Positive	Comments
AST ALT	Unknown, but heavy lasting several weeks	2–4 weeks	Excessive coffee consumption, medications	Ratio of AST: ALT >2:1 suggests liver damage from alcohol. ALT is less sensitive than AST.
GGT	5 drinks/day x several weeks	2–4 weeks	Liver and biliary disease, smoking, obesity, diabetes, hypertension, hypertriglyceridemia	Primarily reflects liver damage, often related to chronic excessive alcohol consumption. More sensitive than AST and ALT.

AST = aspartate amino transferase; ALT = alanine amino transferase; GGT = gamma-glutamyl transferase; CDT = carbohydrate-deficient transferrin; MCV = mean corpuscular volume. \*Indirect serum based biomarkers.

Biomarker (elevated)	Type of Drinking Characterized	Time to Return to Normal with Abstinence	Possible Source of False Positive	Comments
CDT	5 drinks/day x 2 weeks	2–4 weeks	Rare genetic variant, biliary cirrhosis, end stage liver disease, smoking, obesity	Excellent specificity for alcohol misuse, but it is costly. Less sensitive for women and younger age; good biomarker for relapse to heavy drinking. Abnormal range >1.3% total transferrin concentration.
MCV	Unknown, but heavy lasting several months	Up to several months	Hemolysis, bleeding disorders, anemia, folate deficiency, hypothyroidism, hyperglycemia	Poor biomarker for relapse; higher sensitivity in women versus men.

AST = aspartate amino transferase; ALT = alanine amino transferase; GGT = gamma-glutamyl transferase; CDT = carbohydrate-deficient transferrin; MCV = mean corpuscular volume. \*Indirect serum based biomarkers.

## Laboratory Monitoring for Alcohol Use Disorders

### Direct Biomarkers<sup>19–23</sup>

Biomarker	Type of Drinking Characterized	Time to Return to Normal with Abstinence	Possible Source of False Positive	Comments
EtG EtS	May detect a single drink.	1–3 days	Alcohol in medications, hygiene products, etc.	Direct analytes of nonoxidative breakdown of alcohol; sensitive to as little as a single drink; highly sensitive; good indicator of relapse; detected in urine for several days.
PEth	3–4 drinks/day x several days	3 weeks	None likely but still need more data.	Direct serum-based biomarker; linear dose-response relationship; more research is warranted.

EtG = ethyl glucuronide; EtS = ethyl sulfate; PEth = phosphatidyl ethanol.

## Medications for the Treatment of Alcohol Use Disorder<sup>4,26</sup>

Naltrexone C	Naltrexone Oral <sup>4,26</sup>						
C	ose Initiation	Contraindications/Precautions	Baseline Evaluation	Monitoring	Common Side Effects		
Initiation	50 mg daily Alternative dosing: 25 mg 1 or 2 times daily with meals to reduce nausea, especially during the first week	<ul> <li>Cannot be used in patients on opioids</li> <li>Patients with physiologic opioid dependance should be opioid-free (including tramadol) a minimum of 7-14 days</li> </ul>	<ul> <li>LFTs; GGT; Bilirubin</li> <li>Urine</li> <li>beta-HCG for females</li> </ul>	LFTs at 6 months then yearly Suicidal thoughts and	<ul> <li>Abdominal cramps</li> <li>Abdominal pain</li> <li>Nausea</li> <li>Headache</li> </ul>		
Maintenance Special Populations	50-100 mg daily Patients with hepatic or renal impairment may respond to lower doses	<ul> <li>days</li> <li>Do not use in severe hepatic impairment or acute hepatitis</li> </ul>		depression	**Side effects are often transient and go away with time.		

For complete prescribing information, please refer to the package insert for each medication; GGT = gamma-glutamyl transferase; HCG = human chorionic gonadotropin; LFT = liver function tests.

Naltrexone Extended-release Injection <sup>4,26</sup>					
Dose Initiation		Contraindications/Precautions	Baseline Evaluation	Monitoring	Common Side Effects
Initiation	380 mg intramuscular gluteal injection	<ul><li>Same as oral</li><li>Clinic administration</li></ul>	<ul> <li>Same as oral</li> </ul>	LFTs at 6 months then	<ul> <li>Same as oral</li> </ul>
Maintenance	380 mg intramuscular gluteal injection every 4 weeks or once a month	<ul> <li>Kept refrigerated. Allow drug to reach room temperature (about 45 minutes) before preparation.</li> </ul>	<ul> <li>Adequate muscle mass for injection</li> </ul>	yearly Suicidal thoughts and depression	<ul> <li>Injection site reaction</li> <li>**Side effects</li> </ul>
Special Populations	CrCl < 50 mL/min use with caution, no dose adjustment recommended				are often transient and go away with time.

For complete prescribing information, please refer to the package insert for each medication; CrCl = creatinine clearance; LFT = liver function tests.

Topiramate 4,2	Topiramate <sup>4,26</sup>							
Dos	e Initiation	Contraindications/ Precautions	Baseline Evaluation	Monitoring	Common Side Effects			
Initiation	25 mg daily, increase dose by 25–50 mg/ day divided twice daily at weekly intervals	<ul> <li>Caution in patients with history of kidney stones</li> <li>Caution in use with metformin (increased metabolic acidosis risk)</li> <li>Use during pregnancy can</li> </ul>	<ul> <li>Weight</li> <li>CrCl</li> <li>Serum bicarbonate</li> <li>Urine beta- HCG for</li> </ul>	Periodic: renal function, serum bicarbonate Ammonia levels with	<ul> <li>Cognitive/ memory impairment</li> <li>Paresthesia</li> <li>Weight loss</li> <li>Headache</li> </ul>			
Maintenance Special Populations	200 - 300 mg daily CrCl <70 mL/min: Give 50% of dose	<ul> <li>Ose during pregnancy can cause cleft lip or palate</li> <li>May decrease the serum concentrations of contraceptives and reduce their effectiveness</li> </ul>	females	lethargy, vomiting, or changes in mental status Suicidal thoughts and depression	<ul> <li>Fatigue</li> <li>Fatigue</li> <li>Dizziness</li> <li>**Most</li> <li>side effects</li> <li>are dose-</li> <li>dependent and</li> <li>may dissipate</li> <li>over time.</li> </ul>			

\*\*If side effects don't improve after 4-6 weeks, dose reduction is recommended to improve adherence. For complete prescribing information, please refer to the package insert for each medication; CrCl = creatinine clearance; HCG = human chorionic gonadotropin.

Acamprosate 4,26							
Dos	e Initiation	Contraindications/ Precautions	Baseline Evaluation	Monitoring	Common Side Effects		
Initiation and Maintenance	666 mg orally 3 times daily	<ul> <li>Higher pill burden, multiple daily dosing</li> <li>Reduce dose in patients</li> </ul>	<ul> <li>CrCl</li> <li>Urine beta- HCG for</li> </ul>	CrCl in higher-risk patients	<ul> <li>Diarrhea</li> <li>Nervousness</li> <li>Fatigue</li> </ul>		
Special Populations	CrCl 30-50 mL/ min: 333 mg orally 3 times daily CrCl < 30 mL/min: do not use	<ul> <li>Reduce dose in patients with low body weight &lt; 60kg</li> </ul>	<ul> <li>Abstinence</li> <li>&gt;4 days</li> <li>before</li> <li>initiation</li> <li>may</li> <li>improve</li> <li>results</li> </ul>	(elderly, renal impairment) Suicidal thoughts and depression	Faligue     **Side effects     generally subside     with continued     use.		

For complete prescribing information, please refer to the package insert for each medication; CrCl = creatinine clearance; HCG = human chorionic gonadotropin.

Disulfiram <sup>4,26</sup>					
Dose Initiation		Contraindications/Precautions	Baseline Evaluation	Monitoring	Common Side Effects
Initiation	250 mg daily	<ul> <li>Patient must be abstinent prior to therapy (≥12 hrs) and</li> </ul>	<ul><li>LFTs</li><li>CBC</li></ul>	LFTs at 1 month, then	<ul><li>Somnolence</li><li>Metallic taste</li></ul>
Maintenance	250–500 mg daily (range 125–500 mg)	<ul><li>committed to staying sober</li><li>Reaction with alcohol can occur</li></ul>	<ul><li>BMP</li><li>Medical and</li></ul>	monthly for 3 months	<ul><li>Headache</li></ul>
Special Populations	_	<ul> <li>for up to 14 days after last dose</li> <li>Contraindicated in severe myocardial disease, psychosis, cognitive disorders, severe hepatic dysfunction</li> <li>Products containing ethanol could cause disulfiram reaction</li> </ul>	<ul> <li>psychiatric assessment</li> <li>EKG</li> <li>Urine beta- HCG for females</li> </ul>	then periodically thereafter	Major: Hepatotoxicity, peripheral neuropathy, psychosis, delirium

For complete prescribing information, please refer to the package insert for each medication; BMP = basic metabolic panel; CBC = complete blood count; CrCl = creatinine clearance; EKG = electrocardiogram; HCG = human chorionic gonadotropin; LFT = liver function tests.

Gabapentin <sup>4,2</sup>	Gabapentin <sup>4,26</sup>				
Dose Initiation		Contraindications/ Precautions	Baseline Evaluation	Monitoring	Common Side Effects
Initiation	300 mg at bedtime, may increase dose by 300 mg/day daily, given in divided doses	<ul> <li>Misuse potential</li> <li>Use caution with CNS depressants (e.g., opioids, benzodiazepines)</li> </ul>	<ul> <li>CrCl</li> <li>Urine beta- HCG for females</li> </ul>	Suicidal thoughts and depression	<ul><li>Somnolence</li><li>Fatigue</li><li>Dizziness</li><li>Ataxia</li></ul>
Maintenance	Target dose 1800 mg/day in 3 divided doses				<ul> <li>Peripheral edema</li> </ul>
Special Populations	CrCl* = 30 to 59 mL/ min: 400 to 1400 mg/ day given in two divided doses; 15–29 mL/min: 200–700 mg at bedtime				

For complete prescribing information please refer to the package insert for each medication; CrCl = creatinine clearance; HCG = human chorionic gonadotropin.

\*For CrCl < 29 mL/min please see package insert for dosing adjustments.

## Investigational Medications for Treatment of Alcohol Use Disorder<sup>26-31</sup>

	Baclofen	Ondansetron	Varenicline
Dose Initiation	5 mg three times daily	4 mcg/kg twice daily (~0.25 mg twice daily – use liquid solution)	Days 1 to 3: 0.5 mg once daily Days 4 to 7: 0.5 mg twice daily
Maintenance	Most commonly studied dose is 10–20 mg three times daily	4 mcg/kg twice daily	1 mg twice daily
Dosing in Special Populations	<ul> <li>CrCL 50–80 mL/min: Reduce dose by one-third</li> <li>CrCL 30–50 mL/min: Reduce dose by one-half</li> <li>CrCL &lt;30 mL/min: Reduce dose by two-thirds</li> </ul>	<ul> <li>Renal impairment: Dose adjustment not necessary</li> <li>Severe hepatic impairment (Child-Pugh ≥10) = 8 mg/ day max</li> </ul>	<ul> <li>CrCl &lt;30 mL/min: Maximum of 0.5 mg twice daily</li> <li>Hemodialysis: Maximum of 0.5 mg daily if tolerated</li> </ul>

For complete prescribing information please refer to the package insert for each medication; CrCl = creatinine clearance; HCG = human chorionic gonadotropin; LFT = liver function tests.

	Baclofen	Ondansetron	Varenicline
Baseline Evaluation	Urine beta-HCG for females	<ul> <li>EKG if patient high risk for prolonged QT interval – Use clinical judgment with low dose used in AUD</li> <li>Urine beta-HCG for females</li> </ul>	<ul> <li>CrCl</li> <li>Suicidal intent</li> <li>Neuropsychiatric symptoms (e.g., agitation, depression)</li> <li>Urine beta-HCG for females</li> </ul>
Adverse Effects	<ul> <li>Drowsiness</li> <li>Dizziness</li> <li>Ataxia</li> <li>Insomnia</li> <li>Weakness</li> </ul>	<ul> <li>Headache</li> <li>Fatigue</li> <li>Constipation</li> <li>Dizziness</li> <li>Fever</li> </ul>	<ul> <li>Nausea/vomiting</li> <li>Headache</li> <li>Abnormal dreams</li> <li>Constipation</li> </ul>

For complete prescribing information please refer to the package insert for each medication; CrCl = creatinine clearance; HCG = human chorionic gonadotropin; LFT = liver function tests.



## Alcohol Use Disorder and Pregnancy

There is no safe level of alcohol use during pregnancy, and abstinence is recommended.<sup>32-34</sup>

Alcohol consumption during pregnancy is associated with:<sup>32-34</sup>

- Pregnancy complications (miscarriage, preterm labor, placenta abruption)
- · Increased rates of stillbirth and low birth weight
- Cognitive deficits and behavioral problems
- Fetal alcohol spectrum disorders

Alcohol withdrawal needs to be managed in pregnant women. Based on the severity of withdrawal, consider the utilization of benzodiazepines or gabapentin (see pages 27-33 for additional detail). There is limited evidence on the safety of medications to treat AUD in pregnancy. Guidelines recommend that pregnant patients with AUD should preferentially be offered evidence-based psychosocial treatment interventions.<sup>33,34</sup>

In some cases, if psychosocial treatment interventions are insufficient, then potential harms associated with alcohol use in pregnancy should be weighed against the potential risks associated with AUD pharmacotherapy.<sup>32,35</sup>



## Pharmacotherapy for AUD in Pregnancy<sup>32,35</sup>

Drug	Therapeutic Notes
Naltrexone	Limited evidence with naltrexone use in opioid use disorder has demonstrated no adverse effects on pregnancy outcomes. <sup>36–40</sup> However, the long-term effects of antagonizing the endogenous opioid system during development are not well known.
Topiramate	Topiramate should be avoided, if possible, during the first trimester. If required, utilize the lowest effective dose. Use during the first trimester is associated with a two to threefold increased risk of malformations, primarily due to oral clefts. <sup>41</sup> Higher doses used in the third trimester are associated with increased prevalence of small for gestational age infants. <sup>41</sup> Doses of 100 mg/day may not be associated with a significantly increased risk of malformations. <sup>42</sup>
Acamprosate	A retrospective cohort study found that acamprosate-exposed neonates were similar to a non-exposed community comparison group for hospitalizations. The acamprosate group also fared better than the untreated alcohol-exposed comparison group for hospitalizations during pregnancy and 45 days post-partum. No differences were seen between the groups for birth weight, the proportion of small for gestational age neonates, or the incidence of congenital abnormalities. <sup>38</sup>

Drug	Therapeutic Notes
Disulfiram	Sparse evidence suggests that this drug is not a major human teratogen. <sup>41</sup> The negative effects of alcohol on the developing fetus are mediated through acetaldehyde, thus the risks associated with alcohol consumption during pregnancy could be amplified by drinking while on disulfiram. <sup>35</sup>
Gabapentin	Population-based studies found that early exposure was not associated with fetal malformations. There is some indication of a higher risk of cardiac malformations. <sup>43,44</sup> Use, especially late, has been associated with increased risk of preterm birth, small for gestational age infants, and neonatal intensive care admission. <sup>43,44</sup>

### **Breastfeeding and AUD**

There is limited evidence on the safety of maternal use of AUD pharmacotherapy during breastfeeding. Careful assessment of benefits and risks, fully informed patient consent, and close monitoring of the infant is advised.<sup>32</sup>

### Pharmacotherapy for AUD and Breastfeeding

Drug	Therapeutic Notes
Naltrexone <sup>45</sup>	Limited data indicates that naltrexone is minimally excreted in breast milk. No naltrexone-related adverse effects were reported in a 1.5-month-old infant. <sup>45</sup>
Topiramate <sup>46</sup>	In a small number of infants studied, maternal doses up to 200 mg daily produce relatively low levels in infant serum. Watery foamy stools reported in one infant that subsided when topiramate was discontinued. Monitor the infant for diarrhea, drowsiness, irritability, adequate weight gain, and developmental milestones, especially in younger, exclusively breastfed infants.
Acamprosate <sup>41</sup>	No human studies exist. The effect on nursing infants is unknown.
Disulfiram <sup>41</sup>	No human studies exist. The effect on nursing infants is unknown.
Gabapentin <sup>41,47</sup>	Gabapentin is excreted in breast milk. Limited information indicates that maternal doses of gabapentin up to 2.1g daily produce relatively low levels in infant serum. The safety of gabapentin for breastfeeding has been investigated by a few case reports involving a range of doses and treatment durations, and no significant adverse effects were reported. LactMed recommends that the infant is monitored for drowsiness, adequate weight gain, and developmental milestones. <sup>47</sup>

## Alcohol Use Disorder and Hepatitis C (HCV) or B (HBV) and Human Immunodeficiency Virus (HIV) Infections<sup>48</sup>

Alcohol Use Disorder and HCV and/or HIV infections often co-occur.

Infection	Condition
HBV or HCV Without Cirrhosis	<ul> <li>Heavy alcohol use in HBV or HCV is associated with more progressive liver damage, liver cancer, and liver-related deaths.</li> <li>Patients with AUD and HCV should be considered for HCV treatment following assessment of a patient's understanding of treatment goals and provision of education about adherence and follow-up.</li> </ul>
HIV	<ul> <li>Heavy alcohol consumption is associated with lower antiretroviral therapy treatment adherence, lower quality of care, and poor retention in care.</li> <li>Unhealthy alcohol use should be targeted to increase the proportion of HIV/AIDS patients who achieves viral suppression.</li> </ul>
Liver Cirrhosis	<ul> <li>Alcohol use can contribute to an acceleration of liver disease (e.g., alcoholic cirrhosis, acute alcoholic hepatitis).</li> <li>In patients with liver disease, alcohol use can speed disease progression.</li> <li>Alcohol use should be targeted for chronic liver disease management.</li> </ul>

Management

- Patients with AUD should be screened for HCV, HBV, and HIV infections.
- Patients with HCV, HBV, or HIV infections should be screened for AUD.
- Patients with advanced fibrosis/cirrhosis disease should be screened for AUD due to the risk of progression of liver disease.
- Interventions should focus on reducing alcohol consumption, treating HIV, HCV, and HBV infections appropriately, and management of cirrhosis.
- HCV treatment options for patients with cirrhosis are limited, highlighting the importance of screening for AUD to reduce the risk of liver disease progression.

AUD is the most common non-tobacco substance use disorder among Veterans with HCV, with 55% of HCV viremic Veterans suffering from problematic alcohol use.

## Special Considerations for AUD Pharmacotherapy Use in HIV and HCV<sup>49,50</sup>

Considerations	Naltrexone	Disulfiram	Topiramate*	Ondansetron*
Drug Interactions with HIV/ HCV/HBV Medications	No CYP450 interactions.	<ul> <li>Medications that contain alcohol and may precipitate reaction:</li> <li>Ritonavir</li> <li>Lopinavir/ ritonavir oral solution</li> <li>Timpranavir capsules</li> <li>Fosamprenavir oral solution</li> </ul>	Closely monitor renal function with co-administered with Tenofovir Disoproxil Fumarate due to increased risk of renal toxicity.	No known drugs interactions.
Cirrhosis	Avoid in acute Hepatitis or liver failure**.	There are no dosage adjustments provided in the manufacturer's labeling. Use with extreme caution in hepatic cirrhosis or insufficiency.	—	Hepatic impairment, severe (Child-Pugh score 10 or greater): do not exceed 8 mg/day.

\*Not FDA approved to treat AUD; No known drug interactions with HIV/HCV medications and acamprosate, baclofen, gabapentin, ondansetron, or varenicline reported. Practitioners should consult with a knowledgeable clinical pharmacist for additional information.

\*\*Not recommended for patients with signs and symptoms of decompensated cirrhosis including ascites, hepatic encephalopathy, jaundice, variceal bleed, spontaneous bacterial peritonitis (SBP), or hepatorenal syndrome (HRS).

## Psychosocial Interventions<sup>25</sup>

Psychosocial Factors	Twelve-Step Facilitation	Community Reinforcement Approach	Motivational Enhancement Therapy	Cognitive Behavioral Therapy	Behavioral Couples Therapy
Structured or Manual Based	$\checkmark$	$\checkmark$	$\checkmark$	$\checkmark$	$\checkmark$
Usual Length of Treatment	10–12 sessions over 1-month	8–12 sessions over 12–16 weeks	12-weeks	6–12 sessions over 6-months	12 weekly sessions
Requires Specialty Trained Provider	$\checkmark$	$\checkmark$	$\checkmark$	$\checkmark$	$\checkmark$
Goal(s)	Therapy designed to increase 12-step group involvement.	Develop social activities and networks that do not involve alcohol use.	Address ambivalence towards behavior change and develop a patient-initiated change plan.	Focus on relapse prevention skills training to develop healthy alternatives to drinking, cope with cravings and life stressors.	Improve relationships with effective communication and healthy shared activities.

## Outpatient Medically Supervised Withdrawal<sup>4,51-53</sup>

Many patients undergoing alcohol withdrawal can do so safely at home with regular supervision.

Alcohol Withdrawal Assessment	Clinical Institute Wi Assessment from A Revised (CIWA-Ar	Alcohol -
<ul> <li>History and severity of previous episodes of alcohol withdrawal (e.g., level of care, delirium tremens (DT), seizures)</li> <li>History of alcohol use (daily consumption, recent patterns)</li> <li>Time of most recent drink</li> <li>Physical examination</li> <li>Concomitant drugs (illicit, prescribed, over the counter)</li> <li>Co-existing medical/psychiatric disorders</li> <li>CBC, urea, electrolytes, LFTs, INR, prothrombin time, urine</li> </ul>	Scores, combined with a of withdrawal seizures o tremens, are used to cat patient's withdrawal.	or delirium
	Withdrawal	Score
	Very mild withdrawal	<10
	Mild withdrawal	10 to 15
drug screen	Moderate withdrawal	16 to 20
	Severe withdrawal	>20

#### Inpatient Medically Supervised Alcohol Withdrawal Likely Required<sup>4,51–53</sup>

- CIWA-Ar score >15 and/ or regular consumption of >17 standard drinks/day or elevated vitals within 72 hours of abstaining
- History of epilepsy, alcohol-related withdrawal seizures or hallucinations, delirium tremens, or failed community detoxifications
- Concurrent substance misuse and/or risk or withdrawal from other substances in addition to alcohol (e.g., sedative-hypnotics)
- Homeless or has no social support
- Very young, elderly, or pregnant
- Cognitive impairment, psychiatric or medical conditions that would pose a risk (e.g., severe coronary artery disease, congestive heart failure, liver cirrhosis)

### Evaluate for Alcohol Withdrawal in the Community<sup>4,51-53</sup>

- CIWA-Ar 8–15 and without symptoms of delirium tremens
   (DT) or seizures
- No history of DT or alcohol withdrawal seizures
- · Able to take oral medications
- Someone who can monitor and supervise the withdrawal process at home
- · Able to commit to daily medical visits
- No unstable medical condition
- No psychotic, suicidal, or significantly cognitively impaired
- Not pregnant
- No concurrent substance use that may lead to withdrawal (e.g., sedative withdrawal)
- Detailed treatment plan that includes provider contact information and contingency plans
- Medication provided and physical health assessed daily for  $^{\rm 3-5}$  days

## Outpatient Treatment of Alcohol Withdrawal<sup>3,16-18</sup>

	Determine Treatment Setting				
CIWA-Ar	Pharmacotherapy for Withdrawal Symptoms	Treatment Setting			
<10	<ul> <li>Withdrawal medication may not be needed</li> <li>Supportive treatment for somatic symptoms</li> <li>Patients who have had alcohol intake within the previous six to eight hours may not yet exhibit withdrawal</li> </ul>	Community			
10–18	<ul><li>Withdrawal medication often appropriate</li><li>Supportive treatment for somatic symptoms</li></ul>	Community or hospital			
>18 or >10 plus co-morbid alcohol-related problems	<ul> <li>Referral for inpatient withdrawal often appropriate</li> <li>Withdrawal medication required (e.g., benzodiazepine)</li> <li>Supportive treatment for somatic symptoms</li> </ul>	Hospital			

### **Determine Treatment Setting**

#### **Current** intoxication:

- Patients who demonstrate significant withdrawal symptoms with a positive blood alcohol concentration are at high risk of severe withdrawal symptoms within a few hours.
- Patients who present for treatment while intoxicated should be reevaluated after the alcohol concentration is below 0.02 g/dL.

### Binge drinking:

• Patients who report >3 binges (>4 drinks/day) in a week for two consecutive weeks should be closely monitored for the emergence of alcohol withdrawal symptoms.

### Benzodiazepines for the Treatment of Outpatient Alcohol Withdrawal<sup>16-23</sup>

- Benzodiazepines are not only the most extensively studied but have demonstrated greatest efficacy in the treatment of alcohol withdrawal.
- Fixed-dose or symptoms triggered protocols can be utilized based on withdrawal severity and gradually reduced over 5–7 days.
- Benzodiazepine use beyond 5–7 days is rarely helpful or necessary.

Benzodiazepine	Fixed Dosing Examples	
Chlordiazepoxide	25–50 mg every 6 hours x 4 doses, then:	<ul> <li>15–25 mg every 6 hours x 4 doses,</li> <li>then 10 mg every 6 hours x 4 doses,</li> <li>then 5 mg every 6 hours x 4 doses</li> </ul>
Lorazepam*	2–4 mg every 6 hours x 4 doses, then:	<ul> <li>1–2 mg every 6 hours x 4 doses,</li> <li>then 0.5 mg every 6 hours x 8 doses</li> </ul>

### Moderate – Severe (9–14 standard drinks/day) Outpatient Alcohol Withdrawal Dosing Examples

\*Lorazepam or oxazepam should be used in the elderly and with hepatic dysfunction.

### Anticonvulsants for Alcohol Withdrawal

Carbamazepine, gabapentin, and valproic acid can be used as effective supplements or alternatives in patients who cannot use benzodiazepines (e.g., abuse liability or allergy/adverse reactions) for mild to moderate alcohol withdrawal.

Medication	Dosing Examples	
Gabapentin	300–400 mg three times daily x 2 days, then	<ul> <li>300–400 mg twice daily x 2 days,</li> <li>then 300–400 mg daily x 2 days</li> </ul>
Carbamazepine	200 mg four times daily x 4 doses, then	<ul> <li>200 mg three times daily x 3 doses,</li> <li>then 200 mg twice daily x 6 doses</li> </ul>
Valproic acid	500 mg three times daily x 7 days	

### Mild to Moderate Outpatient Alcohol Withdrawal Dosing Examples<sup>4,51,54,55</sup>

The use of non-benzodiazepine agents for alcohol withdrawal management has not been well-studied in patients with either severe alcohol withdrawal (especially a CIWA-Ar >15) or those at risk for complications of withdrawal (seizure, DT, hallucinosis), and thus use in these situations may carry unknown risks and uncertain benefit.

## Treatment Options for Somatic Complaints During Alcohol Withdrawal<sup>53\*</sup>

Symptom	Treatment	
Dehydration	Ensure adequate fluid intake to maintain hydration and electrolyte balance	
Pain	NSAIDs (e.g., ibuprofen), acetaminophen; max 2 gm/day in patients with hepatic impairment	
Nausea and vomiting	Antiemetics (e.g., promethazine 25 mg every 4 hours as needed)	
Diarrhea	Loperamide (4 mg then 2 mg after each loose stool; $max = 16 mg/day$ )	
Itching	Antihistamines (e.g., hydroxyzine 25–50 mg three times daily)	

\*These medications do not prevent seizures.

### Nutritional Supplements to Consider for Patients Going Through Alcohol Withdrawal<sup>51,56</sup>

Supplement	Treatment
Thiamine**	100–300 mg/day x 5 days
Folic acid	0.4–1 mg/day x 5 days
Pyridoxine (B6)	2 mg/day x 5 days

\*\*All patients with AUD should be offered oral thiamine to prevent long term complication.

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