U.S. Department of Veterans Affairs
Veterans Health Administration
PBM Academic Detailing Service

A QUICK REFERENCE GUIDE (2017)

Alcohol Use Disorder

Leading the Charge in the Treatment of Alcohol Use Disorder (AUD)

VA PBM Academic Detailing Service

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http://www.pbm.va.gov/PBM/academicdetailingservicehome.asp

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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.[1,2]

Gender	Single-day Limit	Weekly Limit
Men	≤4 standard-size drinks	≤14 standard-sized drinks
Women or Age >65	≤3 standard-size drinks	≤7 standard-sized drinks

Standard sizes of alcoholic beverages: One standard drink contains 14 grams of alcohol

The percent of "pure alcohol", expressed here as alcohol by volume (alc/vol), varies by beverage.

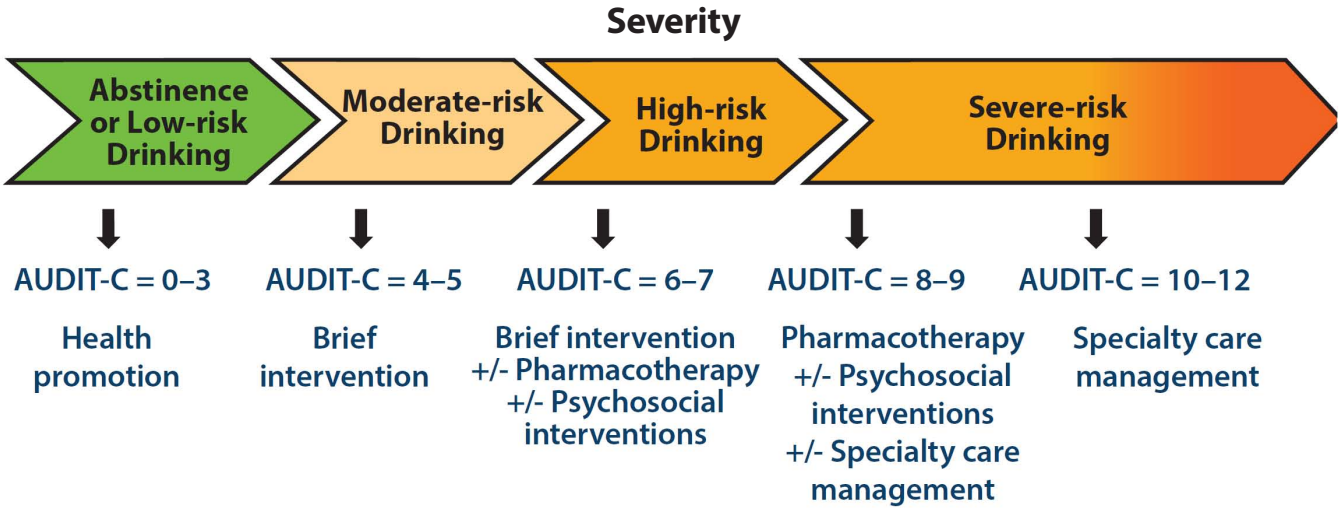
Screening — Alcohol Use Disorders Identification Test (AUDIT-C)[3]

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
How often do you have 6 or more drinks on an occasion in the past year?	Never	Less than monthly	Monthly	Weekly	Daily or almost daily

When the AUDIT-C is administered by self-report add a "0 drinks" response option to question #2 (0 points based on validations studies). In addition, it is valid to input responses of 0 points to questions #2–3 for patients who indicate "never" in response to question #1 (past year non-drinkers).

All Veterans should be screened for alcohol use at least annually.

Spectrum of Unhealthy Alcohol Use with AUDIT-C Score and Recommended Treatment[3–6]



Laboratory Monitoring of Alcohol Biomarkers — How Can They Be Used?[7,8]

Screening tool

- Measuring biomarkers may assist in differential diagnosis
- Alcohol misuse may be missed
- Misuse is high in certain medical contexts (e.g. psychiatry, emergency departments)
- Helps evaluate why medical condition (e.g. hypertension, insomnia) may not be responding to treatment

Motivating change in drinking behavior

- Biomarker measurement can help motivate changes in drinking behaviors

Identifying relapse to drinking

- For example, Carbohydrate-Deficient Transferrin (CDT) elevation can be an early marker
- Addressing relapse early can prevent further alcohol misuse

Laboratory Monitoring for Alcohol Use Disorders: Indirect Biomarkers[8,9]

Biomarker*	Type of Drinking Characterized	Time to Return to Normal with Abstinence	Possible Source of False Positive	Comments
AST	Unknown, but heavy lasting several weeks	2–4 weeks	Excessive coffee consumption, medications	Ratio AST:ALT >2:1 suggests liver damage from alcohol.
ALT				ALT 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 alcohol.
CDT	5 drinks/day x 2 weeks	2–4 weeks	Rare genetic variant, biliary cirrhosis, end stage liver disease, smoking, obesity	Less sensitive for women and younger age; good biomarker for relapse to heavy drinking.

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

continued from page 5 (Laboratory Monitoring for Alcohol Use Disorders: Indirect Biomarkers)

Biomarker*	Type of Drinking Characterized	Time to Return to Normal with Abstinence	Possible Source of False Positive	Comments
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[7,8]

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.
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.

Example of a Brief Intervention[6,7]

(Example available at: **https://www.youtube.com/watch?v=b-ilxvHZJDc**)

Brief Intervention	Example Language
Raise the subject about patient's risk for drinking related health problems.	*"I am concerned about your use of alcohol because you are drinking above the recommended limits."*
Provide feedback on links between alcohol use and patient's ***co-occuring health conditions*** (if present), such as diabetes, hypertension, depression, anxiety, insomnia, pain, GI problems (GERD), fractures, obesity, sexual dysfunction & peripheral neuropathy.	*"Because of your [chronic or co-occuring condition], I am concerned that your alcohol use may impact your health by [relevant repercussion]."*
Provide ***explicit advice*** to cut down and ***enhance motivation*** to change and decrease or abstain from alcohol use. If patient indicates no desire to change, provide information handout.	*"What do you see as the possible benefits to cutting down?"* *"What would be a reason to you that change would be worth considering?"*
Negotiate a plan to set a feasible drinking goal and arrive at ***a shared decision***. Encourage specificity (e.g., cutting down to X number of drinks and documenting intended steps).	*"What changes are you willing to make to meet this goal?"*
Suggest treatment referral, if appropriate (e.g., AUDIT-C ≥8).	*"Would you be willing to talk to one of my colleagues to learn about options to support your changes?"*

FDA Approved Medications for the Treatment of Alcohol Use Disorder[3,9,10]

	Naltrexone Oral**	Naltrexone Extended-release Injection	Acamprosate	Disulfiram*
Clinical Pearls	• Effective at: ↓ drinking ↓ cravings ↑ abstinence	• Same efficacy as oral naltrexone; may benefit patients with adherence issues	• Effective at: ↑ abstinence • More effective for patients with a goal of abstinence	• More effective for patients with a goal of abstinence and with monitored administration • Reaction with alcohol can occur for up to 14 days after last dose

For complete prescribing information please refer to the package insert for each medication; BMP = basic metabolic panel; CBC = complete blood count; Cmax = maximum concentration; CrCl = creatinine clearance; EKG = electrocardiogram; GGT = gamma-glutamyl transferase; HCG = human chorionic gonadotropin; IM = intramuscular; LFT = liver function tests; TCA = tricyclic antidepressant; *Possible role in comorbid AUD and Cocaine Use Disorder; **Side effects are often transient and go away with time.

continued from page 9 (FDA Approved Medications for the Treatment of Alcohol Use Disorder)

	Naltrexone Oral**	Naltrexone Extended-release Injection	Acamprosate	Disulfiram*
Contraindications	• Concomitant opioids (including tramadol) • Acute hepatitis or liver failure • Opioid dependence or use within past 7 days	• Concomitant opioids • Acute hepatitis or liver failure • Opioid dependence or use within past 7 days	• CrCl ≤30 mL/min	• Severe myocardial disease • Severe hepatic dysfunction • Use of alcohol or alcohol containing products • Concomitant or recent use of metronidazole or ketoconazole • Psychoses, cognitive disorders, suicidal ideation

For complete prescribing information please refer to the package insert for each medication; BMP = basic metabolic panel; CBC = complete blood count; Cmax = maximum concentration; CrCl = creatinine clearance; EKG = electrocardiogram; GGT = gamma-glutamyl transferase; HCG = human chorionic gonadotropin; IM = intramuscular; LFT = liver function tests; TCA = tricyclic antidepressant; *Possible role in comorbid AUD and Cocaine Use Disorder; **Side effects are often transient and go away with time.

continued from page 9 (FDA Approved Medications for the Treatment of Alcohol Use Disorder)

	Naltrexone Oral**	Naltrexone Extended-release Injection	Acamprosate	Disulfiram*
Baseline Evaluation	• Opioid free ≥7–10 days • LFTs; GGT; Bilirubin • Urine beta-HCG for females • Abstinence ≥4 days prior to initiation may improve results	• Opioid free ≥7–10 days • LFTs; GGT; Bilirubin • Urine beta-HCG for females • CrCl ≥50 mL/min • Adequate muscle mass for injection	• CrCl • Urine beta-HCG for females • Abstinence ≥4 days prior to initiation may improve results	• Must be alcohol free ≥12 hrs and blood alcohol level = 0 • LFTs, CBC, BMP • Medical and psychiatric assessment • EKG • Urine beta-HCG for females • Consider utilizing a consent form

For complete prescribing information please refer to the package insert for each medication; BMP = basic metabolic panel; CBC = complete blood count; Cmax = maximum concentration; CrCl = creatinine clearance; EKG = electrocardiogram; GGT = gamma-glutamyl transferase; HCG = human chorionic gonadotropin; IM = intramuscular; LFT = liver function tests; TCA = tricyclic antidepressant; *Possible role in comorbid AUD and Cocaine Use Disorder; **Side effects are often transient and go away with time.

continued from page 9 (FDA Approved Medications for the Treatment of Alcohol Use Disorder)

	Naltrexone Oral**	Naltrexone Extended-release Injection	Acamprosate	Disulfiram*
Dose Initiation	• 50 mg daily Alternative dosing: • 25 mg 1 or 2 time(s) daily with meals to reduce nausea, especially during the first week	• 380 mg IM monthly	• 666 mg three times daily	• 250 mg daily
Maintenance	• 50–100 mg daily	• 380 mg IM monthly	• 666 mg three times daily	• Average dose 250–500 mg daily (range 125–500 mg)

For complete prescribing information please refer to the package insert for each medication; BMP = basic metabolic panel; CBC = complete blood count; Cmax = maximum concentration; CrCl = creatinine clearance; EKG = electrocardiogram; GGT = gamma-glutamyl transferase; HCG = human chorionic gonadotropin; IM = intramuscular; LFT = liver function tests; TCA = tricyclic antidepressant; *Possible role in comorbid AUD and Cocaine Use Disorder; **Side effects are often transient and go away with time.

continued from page 9 (FDA Approved Medications for the Treatment of Alcohol Use Disorder)

	Naltrexone Oral**	Naltrexone Extended-release Injection	Acamprosate	Disulfiram*
Dosing in Special Populations	• Patients with hepatic or renal impairment may respond to lower doses	• CrCL 50–80: No dosage adjustments necessary • Uncertain effects CrCL <50	• CrCl 30–50: 333 mg three times daily • CrCl ≤30: Not recommended	• Not applicable
Adverse Effects	• Nausea/ vomiting • Headache • Insomnia • Dizziness • Anxiety • Depression/ dysphoria	• Same as oral • Injection site reaction (pain, pruritus, tenderness, bruising, induration, swelling)	• Diarrhea • Insomnia • Anxiety • Depression • Weakness	• Headache • Metallic or garlic-like aftertaste • Somnolence • Psychosis • Rash • Hepatotoxicity

For complete prescribing information please refer to the package insert for each medication; BMP = basic metabolic panel; CBC = complete blood count; Cmax = maximum concentration; CrCl = creatinine clearance; EKG = electrocardiogram; GGT = gamma-glutamyl transferase; HCG = human chorionic gonadotropin; IM = intramuscular; LFT = liver function tests; TCA = tricyclic antidepressant; *Possible role in comorbid AUD and Cocaine Use Disorder; **Side effects are often transient and go away with time.

continued from page 9 (FDA Approved Medications for the Treatment of Alcohol Use Disorder)

	Naltrexone Oral**	Naltrexone Extended-release Injection	Acamprosate	Disulfiram*
Monitoring	• LFTs at 6 months then yearly	• LFTs at 6 months then yearly	• CrCl in higher risk patients (elderly, renal impairment) • Monitor for suicidal thoughts and depression	• LFTs at 1 month, then monthly for 3 months then periodically there after

For complete prescribing information please refer to the package insert for each medication; BMP = basic metabolic panel; CBC = complete blood count; Cmax = maximum concentration; CrCl = creatinine clearance; EKG = electrocardiogram; GGT = gamma-glutamyl transferase; HCG = human chorionic gonadotropin; IM = intramuscular; LFT = liver function tests; TCA = tricyclic antidepressant; *Possible role in comorbid AUD and Cocaine Use Disorder; **Side effects are often transient and go away with time.

continued from page 9 (FDA Approved Medications for the Treatment of Alcohol Use Disorder)

	Naltrexone Oral**	Naltrexone Extended-release Injection	Acamprosate	Disulfiram*
Drug Interactions	• Opioid containing medications	• Opioid containing medications	• Naltrexone: ↑ Cmax of acamprosate (no dosage adjustment required)	• Alcohol containing medications • ↑ levels of warfarin, phenytoin, TCAs, clozapine, isoniazid, benzodiazepines, methadone, theophyline • ↑ CNS toxicity (i.e. psychosis) with metronidazole

For complete prescribing information please refer to the package insert for each medication; BMP = basic metabolic panel; CBC = complete blood count; Cmax = maximum concentration; CrCl = creatinine clearance; EKG = electrocardiogram; GGT = gamma-glutamyl transferase; HCG = human chorionic gonadotropin; IM = intramuscular; LFT = liver function tests; TCA = tricyclic antidepressant; *Possible role in comorbid AUD and Cocaine Use Disorder; **Side effects are often transient and go away with time.

Non-FDA Approved Medications Supported by Evidence and Guidelines for Treatment of Alcohol Use Disorder[3,9]

	Topiramate	Gabapentin
Clinical Pearls	• Effective at: ↓ drinking ↓ cravings ↑ abstinence • Topiramate is at least as effective as naltrexone and acamprosate.	• Effective alone or in combination with naltrexone at: ↓ drinking ↓ cravings ↓ insomnia ↑ abstinence ↓ acute/protracted withdrawal symptoms such as anxiety • Second line treatment option; use if first-line pharmacotherapy is contraindicated or not effective/tolerated.

For complete prescribing information please refer to the package insert for each medication; AUD = alcohol use disorder; BMP = basic metabolic panel; Cmax = maximum concentration; CrCl = creatinine clearance; EKG = electrocardiogram; GGT = gamma-glutamyl transferase; HCG = human chorionic gonadotropin; LFT = liver function tests; TCA = tricyclic antidepressant.

continued from page 16 (Non-FDA Approved Medications Supported by Evidence and Guidelines for Treatment of Alcohol Use Disorder)

	Topiramate	Gabapentin
Contraindications	• History of renal stones	• Hypersensitivity to gabapentin
Baseline Evaluation	• Weight • CrCl • Serum bicarbonate • Urine beta-HCG for females	• CrCl • Urine beta-HCG for females
Dose Initiation	• 25 mg daily, increase dose by 25–50 mg/day divided twice daily at weekly intervals	• 300 mg at bedtime, may increase dose by 300 mg/day on a daily basis, given in divided doses
Maintenance	• Maxium recommended dose 200 mg/day divided doses • Doses studied range between 75–300 mg/day divided doses	• Target dose 1800 mg/day in 3 divided doses

For complete prescribing information please refer to the package insert for each medication; AUD = alcohol use disorder; BMP = basic metabolic panel; Cmax = maximum concentration; CrCl = creatinine clearance; EKG = electrocardiogram; GGT = gamma-glutamyl transferase; HCG = human chorionic gonadotropin; LFT = liver function tests; TCA = tricyclic antidepressant.

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	Topiramate	Gabapentin
Dosing in Special Populations	• CrCl <70 mL/min: Give 50% of dose and use slower titration • Hepatic impairment: Clearance may be reduced	• CrCl = 15–29 mL/min: 200–700 mg at bedtime • Hemodialysis: CrCl 15 mL/min, 100 to 300 mg/day given once daily; CrCl <15 mL/min, reduce daily dose in proportion to CrCl
Adverse Effects	• Dizziness/ataxia • Paresthesia • Somnolence • Weight loss/anorexia • Psychomotor slowing • Difficulty concentrating • Depression	• Somnolence/fatigue • Dizziness • Ataxia • Peripheral edema • Nystagmus

For complete prescribing information please refer to the package insert for each medication; AUD = alcohol use disorder; BMP = basic metabolic panel; Cmax = maximum concentration; CrCl = creatinine clearance; EKG = electrocardiogram; GGT = gamma-glutamyl transferase; HCG = human chorionic gonadotropin; LFT = liver function tests; TCA = tricyclic antidepressant.

continued from page 16 (Non-FDA Approved Medications Supported by Evidence and Guidelines for Treatment of Alcohol Use Disorder)

	Topiramate	Gabapentin
Monitoring	• Weight, eating behavior • Suicidality • Hydration status, electrolytes • Ammonia levels if unexplained lethargy, vomiting, or changes in mental status • Serum bicarbonate level in patient is experiencing hyperventilation, fatigue, anorexia, cardiac arrhythmias or stupor	• CrCl • Monitor for suicidal thoughts and depression
Drug Interactions	• May reduce effectiveness of oral contraceptives • Divalproex: ↑ risk of hyperammonemia • Carbonic anhydrase inhibitors: ↑ risk renal stones • Carbamazepine, phenytoin, phenobarbital ↓ topiramate levels • Topiramate ↑ levels phenytoin	• Avoid antacid use within two hours of taking gabapentin • Concomitant morphine may ↑ gabapentin levels • Increased sedation with concurrent alcohol or CNS depressants

For complete prescribing information please refer to the package insert for each medication; AUD = alcohol use disorder; BMP = basic metabolic panel; Cmax = maximum concentration; CrCl = creatinine clearance; EKG = electrocardiogram; GGT = gamma-glutamyl transferase; HCG = human chorionic gonadotropin; LFT = liver function tests; TCA = tricyclic antidepressant.

Non-FDA Approved Investigational Medications for Treatment of Alcohol Use Disorder[9,11,12]

	Baclofen	Ondansetron	Varenicline
Clinical Pearls	• May be effective at: ↓ drinking ↓ cravings ↑ abstinence • Might be useful in patients with cirrhosis or liver impairment who do not respond to or can't tolerate acamprosate or gabapentin.	• May be more effective for patients with early onset AUD (<25 yo): ↓ drinking ↓ cravings ↑ abstinence • Not enough evidence at this time to define role in AUD treatment.	• May be effective at: ↓ drinking ↓ cravings • Might be useful in patients with comorbid Nicotine Use Disorder who have failed or do not tolerate first or second-line pharmacotherapy options.
Contraindications	• Hypersensitivity to baclofen	• Hypersensitivity to ondansetron or any other selective 5HT3 antagonist	• Hypersensitivity to varenicline

For complete prescribing information please refer to the package insert for each medication; BMP = basic metabolic panel; Cmax = maximum concentration; CrCl = creatinine clearance; EKG = electrocardiogram; GGT = gamma-glutamyl transferase; HCG = human chorionic gonadotropin; LFT = liver function tests; TCA = tricyclic antidepressant.

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	Baclofen	Ondansetron	Varenicline
Baseline Evaluation	• None needed • Urine beta-HCG for females	• Magnesium and potassium level (↑ risk of QT prolongation with low electrolyte levels) – Use clinical judgement with low dose utilized for AUD • EKG if patient high risk for prolonged QT interval – Use clinical judgment with low dose used in AUD • Urine beta-HCG for females	• CrCl • Suicidal intent • Neuropsychiatric symptoms (e.g. agitation, depression, suicidal ideation or behavior) • Urine beta-HCG for females
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

For complete prescribing information please refer to the package insert for each medication; BMP = basic metabolic panel; Cmax = maximum concentration; CrCl = creatinine clearance; EKG = electrocardiogram; GGT = gamma-glutamyl transferase; HCG = human chorionic gonadotropin; LFT = liver function tests; TCA = tricyclic antidepressant.

continued from page 20 (Non-FDA Approved Investigational Medications for Treatment of Alcohol Use Disorder)

	Baclofen	Ondansetron	Varenicline
Maintenance	• Most commonly studied dose is 10–20 mg three times daily	• 4 mcg/kg twice daily (~0.25 mg twice daily – use liquid solution)	• 1 mg twice daily
Dosing in Special Populations	Renal dysfunction: • CrCL 50–80 mL/min: Reduce dose by one-third • CrCL 30–50 mL/min: Reduce does by one-half • CrCL <30 mL/min: Reduce dose by two-thirds	• Renal impairment: Dose adjustment not necessary • Severe hepatic impairment (Child-Pugh ≥10) = 8 mg/day max	• CrCl <30 mL/min: Maximum of 0.5 mg twice daily • Hemodialysis: Maximum of 0.5 mg daily if tolerated • Hepatic impairment: No adjustments needed

For complete prescribing information please refer to the package insert for each medication; BMP = basic metabolic panel; Cmax = maximum concentration; CrCl = creatinine clearance; EKG = electrocardiogram; GGT = gamma-glutamyl transferase; HCG = human chorionic gonadotropin; LFT = liver function tests; TCA = tricyclic antidepressant.

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	Baclofen	Ondansetron	Varenicline
Adverse Effects	• Drowsiness • Dizziness • Ataxia • Insomnia • Weakness	• Headache • Fatigue • Constipation • Dizziness • Fever	• Nausea/vomiting • Headache • Abnormal dreams • Constipation • Insomnia • Irritability • Suicidal ideation • Depression

For complete prescribing information please refer to the package insert for each medication; BMP = basic metabolic panel; Cmax = maximum concentration; CrCl = creatinine clearance; EKG = electrocardiogram; GGT = gamma-glutamyl transferase; HCG = human chorionic gonadotropin; LFT = liver function tests; TCA = tricyclic antidepressant.

continued from page 20 (Non-FDA Approved Investigational Medications for Treatment of Alcohol Use Disorder)

	Baclofen	Ondansetron	Varenicline
Monitoring	• Monitor for psychiatric disturbances and insomnia	• BMP (electrolytes) • QTc (electrolyte abnormalities, congestive heart failure, or concomitant use of QTc prolonging medications) • Signs of serotonin syndrome	• Changes in behavior or thinking • Suicidal ideation or behavior

For complete prescribing information please refer to the package insert for each medication; BMP = basic metabolic panel; Cmax = maximum concentration; CrCl = creatinine clearance; EKG = electrocardiogram; GGT = gamma-glutamyl transferase; HCG = human chorionic gonadotropin; LFT = liver function tests; TCA = tricyclic antidepressant.

continued from page 20 (Non-FDA Approved Investigational Medications for Treatment of Alcohol Use Disorder)

	Baclofen	Ondansetron	Varenicline
Drug Interactions	• Other CNS depressants may enhance CNS effects	• Apomorphine (avoid) • Drugs that prolong QT interval (use caution)	• May enhance the adverse/toxic effects of alcohol • May enhance the adverse/toxic effects of nicotine • H2-Antagonists, quinolone antibiotics and trimethoprim may increase the serum concentration of varenicline

For complete prescribing information please refer to the package insert for each medication; BMP = basic metabolic panel; Cmax = maximum concentration; CrCl = creatinine clearance; EKG = electrocardiogram; GGT = gamma-glutamyl transferase; HCG = human chorionic gonadotropin; LFT = liver function tests; TCA = tricyclic antidepressant.

Alcohol Use Disorder and Hepatitis C (HCV) and Human Immunodeficiency Virus (HIV) Infections[13]

Alcohol Use Disorder and HCV and/or HIV Infections Often Co-Occur	
HCV	• Alcohol use in HCV is associated with more progressive HCV-related liver damage, liver cancer, and liver-related deaths • Patients with AUD and HCV should be considered for HCV treatment on a case-by-case basis based on the likelihood of adherence with medical recommendations, clinic visits, and medications
HIV	• Heavy alcohol consumption is associated with lower antiretroviral therapy treatment adherence, lower quality of care and poor retention in care • Unhealthy alcohol use should be targeted to increase the proportion of HIV/AIDS patient who achieve viral suppression
Liver Disease	• Heavy alcohol use can contribute to acceleration of liver disease (e.g. alcoholic cirrhosis, acute alcoholic hepatitis) • In patients with liver disease, alcohol use can speed disease progression • Alcohol use should be targeted for chronic liver disease management

continued from page 26 (Alcohol Use Disorder and Hepatitis C (HCV) and Human Immunodeficiency Virus (HIV) Infections)

Management

- Patients with AUD should be screened for HCV and HIV infections.
- Patients with HCV and HIV infections should be screened for AUD.
- Patients with chronic liver disease should be screened for AUD.
- Interventions should focus on reducing alcohol consumption, treating viral infections, and management of chronic liver diseases.

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[14,15]

	Naltrexone	Acamprosate	Disulfiram	Topiramate*	Gabapentin*
Drug Interactions with HIV/HCV Medications	No CYP450 interactions.	No known drug interactions.	• Etravirine – disulfiram may increase etravirine levels • Medications that contain alcohol and may precipitate reaction - Ritonavir, lopinavir/ritonavir timpranavir, fosamprenavir capsules/oral solution may contain alcohol in formulation - Peg-interferon alfa	May decrease rilpivirine levels.	No known drugs interactions.

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

continued from page 28 (Special Considerations for AUD Pharmacotherapy Use in HIV and HCV)

	Naltrexone	Acamprosate	Disulfiram	Topiramate*	Gabapentin*
Other Considerations	Avoid in acute hepatitis or liver failure.		• Avoid agents with overlapping risk of peripheral neuropathy • Contraindicated in severe hepatic dysfunction: transaminases >3x upper level of normal	Potential increase risk of renal toxicity with indinavir and tenofovir-TD. Recommend increased monitoring of renal function or switch to emtricitabine/ TAF (tenofovir alfenamide).	

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

Psychosocial Interventions[3]

	Twelve-Step Facilitation	Community Reinforcement Approach	Motivational Enhancement Therpay	Cognitive Behavioral Therapy	Behavioral Couples Therapy
Structured or Manual Based	✓	✓	✓	✓	✓
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	✓	✓	✓	✓	✓
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 patient-initiated change plan.	Focus on relapse prevention skills training to develop healthy alternatives to drinking, cope with cravings and life stressors.	Improve relationship with effective communication and healthy shared activities.

Outpatient Medically Supervised Withdrawal[3,16,17]

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

Alcohol Withdrawal Assessment	Management of Alcohol Withdrawal in the Community
• **History and severity of previous episodes of alcohol withdrawal (e.g. level of care, delirium tremens (DTs), seizures)** • **Severity of dependence** • Physical examination • Time of most recent drink • Concomitant drugs (illicit, prescribed, over the counter) • Co-existing medical/psychiatric disorders • CBC, urea, electrolytes, LFTs, INR, prothrombin time, urine drug screen	• CIWA-Ar 8–15 and without symptoms of 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 abuse 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 3–5 days

continued from page 31 (Outpatient Medically Supervised Withdrawal)

Inpatient Medically Supervised Alcohol Withdrawal Recommended

- Regular consumption of >17 standard drinks/day and/or severe alcohol withdrawal CIWA-Ar score >15; 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 risk (e.g. severe coronary artery disease, congestive heart failure, liver cirrhosis)

Outpatient Treatment of Alcohol Withdrawal[3,16–18]

Determine Treatment Setting		
CIWA-Ar	**Pharmacotherapy for Withdrawal Symptoms**	**Treatment Setting**
<8	• Withdrawal medication may not be needed • Supportive treatment for somatic symptoms • **Patients who have had alcohol intake within the previous six to eight hours may not yet exhibit withdrawal**	Community
8–15	• Withdrawal medication often appropriate • Supportive treatment for somatic symptoms	Community
>15	• Referral for inpatient withdrawal often appropriate • Withdrawal medication required (e.g. benzodiazepine) • Supportive treatment for somatic symptoms	Hospital

continued from page 33 (Outpatient Treatment of Alcohol Withdrawal)

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.

Medications options for the treatment of outpatient alcohol withdrawal[16–23]

- 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
- Benzodiazepine use is not recommended after withdrawal phase

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

Treatment Options for Somatic Complaints During Alcohol Withdrawal[16]

Symptom	Treatment
Dehydration	• Ensure adequate fluid intake to maintain hydration and electrolyte balance
Pain	• Acetaminophen; max 2 gm/day in patients with hepatic impairment
Nausea and vomiting	• Antiemetics (e.g. prochlorperazine 5–10 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)

Medications Options for the Treatment of Outpatient Alcohol Withdrawal[16–23]

Moderate (9–14 standard drinks/day) Outpatient Alcohol Withdrawal Dosing Examples	
Medication	**Dosing Examples**
Benzodiazepine*	Chlordiazepoxide: 25–50 mg every 6 hours x 4 doses, then 15–25 mg every 6 hours x 4 doses, then 10 mg every 6 hours x 4 doses, then 5 mg every 6 hours x 4 doses Lorazepam: 2–4 mg every 6 hours x 4 doses, then 1–2 mg every 6 hours x 4 doses, then 0.5 mg every 6 hours x 8 doses
Carbamazepine	200 mg four times daily x 4 doses, then 200 mg three times daily x 3 doses, then 200 mg twice daily x 6 doses

*Lorazepam or oxazepam preferred in hepatic dysfunction; **All patients with AUD should be offered oral thiamine to prevent long term complications; **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, DTs, hallucinosis), and thus use in these situations may carry unknown risks and uncertain benefit**.

continued from page 36 (Medications Options for the Treatment of Outpatient Alcohol Withdrawal)

Moderate (9–14 standard drinks/day) Outpatient Alcohol Withdrawal Dosing Examples	
Medication	**Dosing Examples**
Gabapentin	300–400 mg three times daily x 2 days, then 300–400 mg twice daily x 2 days, then 300–400 mg daily x 2 days
Valproic acid	500 mg three times daily x 7 days
Nutritional Supplements to Consider for Patients Going Through Alcohol Withdrawal	
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

*Lorazepam or oxazepam preferred in hepatic dysfunction; **All patients with AUD should be offered oral thiamine to prevent long term complications; **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, DTs, hallucinosis), and thus use in these situations may carry unknown risks and uncertain benefit**.

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This reference guide was created to be used as a tool for VA providers and is available to use from the Academic Detailing SharePoint. These are general recommendations only; specific clinical decisions should be made by the treating provider based on an individual patient's clinical condition.

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