


 Providers
Clinical Support
System

Alcohol Use Disorder

Shanna Diaz DO

Psychiatry, Geriatric Psychiatry, and Sleep Medicine
Medical and Fellowship Director of Sleep Medicine
University of New Mexico Hospital

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   Providers
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System 1

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Disclosures

- **No disclosures**

*The content of this activity may include discussion of off label or investigative drug uses.
The faculty is aware that is their responsibility to disclose this information.*

   Providers
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System 2

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Target Audience

- The overarching goal of PCSS is to train healthcare professionals in evidence-based practices for the prevention and treatment of opioid use disorders, particularly in prescribing medications, as well for the prevention and treatment of substance use disorders.
- The Fundamentals of Addiction Medicine ECHO (FAME) series is for physicians, physician assistants, nurse practitioners, nurses, and behavioral health specialists. It is designed for those new to treating patients with addiction and for individuals who have had little or no addiction training.

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Educational Objectives

At the conclusion of this activity participants should be able to:

- Define Alcohol Use Disorder (AUD)
- Review alcohol use epidemiology and risk factors
- Assess for alcohol use in the clinical setting
- Identify alcohol withdrawal
- Review medications for treatment of Alcohol Use Disorder

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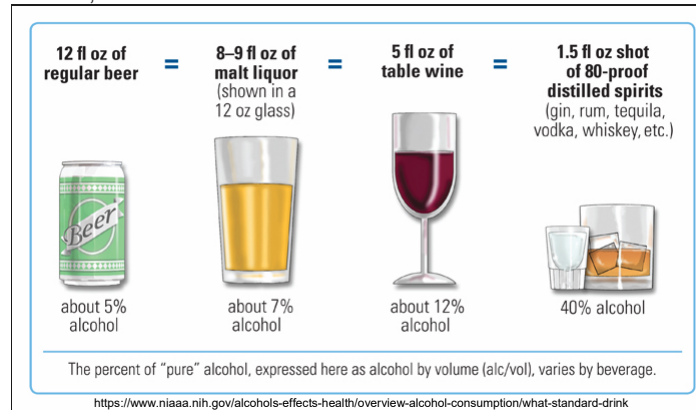
Case

- A 24 year old male reports that he was drinking a 6 pack of beer each weekend since age 21.
- Over the last 4 months he drinks at least a 6 pack each weekend night.
- He recently got a DUI after driving home from his friends house, and now has a suspended license.
- He makes less money now that he can't make deliveries for work.
- His wife is annoyed that he still spends money on beer and that she has to drive him to work now.
- He stopped drinking for a few consecutive weekends, but really looks forward to "letting loose" on the weekends. He plans to try and cut back on the amount he drinks.
 - Does he have a "problem" with alcohol (as his wife says?)
 - How much is "too much" to drink?

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What is a Standard Drink?

- In the U.S., a standard drink contains roughly 14 grams of pure alcohol, which is found in:



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Drinking Levels Defined

Moderate Alcohol Consumption:

- Up to 1 drink per day for women and adults \geq 65 years of age
- Up to 2 drinks per day for men
 - "Dietary Guidelines for Americans 2015-2020," U.S. Department of Health and Human Services and U.S. Department of Agriculture

Risk for developing AUD:

- Women and \geq 65 years of age:
 - > 3 drinks on any single day or > 7 drinks per week
- Men:
 - > 4 drinks on any single day or > 14 drinks per week

Heavy Drinking:

- 5 or more drinks on the same occasion on each of 5 or more days in the past 30 days
 - Substance Abuse and Mental Health Services Administration

Binge Drinking:

- A pattern of drinking that brings blood alcohol concentration (BAC) levels to 0.08g/dl
- 4 drinks for women, 5 drinks for men in about 2 hours
 - National Institute of Alcohol Abuse and Alcoholism

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Alcohol Use and Short Term Health Risks

- Injuries: motor vehicle crashes, falls, drownings, and burns
- Violence: homicide, suicide, sexual assault, and intimate partner violence
- Alcohol poisoning
- Risky sexual behaviors
- Miscarriage and stillbirth or fetal alcohol spectrum disorders (FASDs) among pregnant women

<https://www.cdc.gov/alcohol/fact-sheets/alcohol-use.htm>

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Alcohol Use and Long Term Health Risks

- High blood pressure, heart disease, stroke, liver disease, and digestive problems
- Cancer of the breast, mouth, throat, esophagus, liver, and colon
- Learning and memory problems, including seizure disorders, dementia and poor school performance

<https://www.cdc.gov/alcohol/fact-sheets/alcohol-use.htm>

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Alcohol Use is Associated with Mental Health Co-morbidities

- Depression
 - Meta-analysis of 400,000 participants showed an association between AUD and suicidal ideation, attempt and completion
 - Lifetime rate of suicide attempts among frequent alcohol users in US was 7% vs 1% in general population
- Anxiety
- PTSD
- eating disorders
- sleep disturbances
- other substance use disorders

<https://www.cdc.gov/alcohol/fact-sheets/alcohol-use.htm>

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What is Alcohol Use Disorder?

- A chronic relapsing brain disease
- Impaired ability to stop or control alcohol use despite adverse social, occupational, or health consequences
- Can range from mild to severe
- Recovery is possible regardless of severity
- Per DSM-5: "A problematic pattern of alcohol use leading to clinically significant impairment or distress, as manifested by at least two of the following 11 criteria, occurring within a 12-month period:"

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DSM-5 Criteria for AUD Diagnosis

- Mild = 2-3
 - Moderate = 4-5
 - Severe = 6+
 - Modifiers: Early remission (3-12 months), sustained remission (> 12 months), "controlled environment"
1. Alcohol is often taken in larger amounts or over a longer period than was intended.
 2. There is a persistent desire or unsuccessful efforts to cut down or control alcohol use.
 3. A great deal of time is spent in activities necessary to obtain alcohol, use alcohol, or recover from its effects.
 4. Craving, or a strong desire or urge to use alcohol
 5. Recurrent alcohol use resulting in a failure to fulfill major role obligations at work, school, or home.
 6. Continued alcohol use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of alcohol.
 7. Important social, occupational, or recreational activities are given up or reduced because of alcohol use.
 8. Recurrent alcohol use in situations in which it is physically hazardous.
 9. Alcohol use is continued despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by alcohol.
 10. Tolerance, as defined by either of the following: a) A need for markedly increased amounts of alcohol to achieve intoxication or desired effect b) A markedly diminished effect with continued use of the same amount of alcohol.
 11. Withdrawal, as manifested by either of the following: a) The characteristic withdrawal syndrome for alcohol (refer to criteria A and B of the criteria set for alcohol withdrawal) b) Alcohol (or a closely related substance, such as a benzodiazepine) is taken to relieve or avoid withdrawal symptoms.

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Risk Factors for AUD

- Age of Onset
 - Onset prior age 15 are 4 times more likely to develop alcohol dependence
 - Binge drinking more common in 18-34 y/o
 - Binge drinking more frequent in > 65 y/o
 - 4-5 times a month
- Race:
 - Native American > Caucasian > Hispanic > African American
- Sex:
 - M > F
 - Males are 2x more likely to binge drink
 - Rates of female alcohol consumption on the rise
- Familial Transmission
 - Multifactorial
 - Genetic, biologic, social, cultural, environmental

www.cdc.gov National Center for Chronic Disease Prevention and Health Promotion, Division of Population Health, Alcohol and Public Health
<https://www.webmd.com/women/news/20180718/alcohol-consumption-among-women-is-on-the-rise>

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Prevalence of Alcohol Use Disorder

- Lifetime AUD prevalence of **29.1%**
- 12-month prevalence of **13.9%**.
- Prevalence of severe AUD greatest among respondents with the lowest incomes
 - multifactorial
- Only 19.8% of respondents with lifetime AUD were ever treated

"Epidemiology of DSM-5 Alcohol Use Disorder". Published in JAMA Psychiatry June 2015. N = 36,309 adults

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Screening for AUD in the Clinical Setting

Single-item screening

- Brief, requires no scoring
- **How many times in the past year have you had five (four for women) or more drinks in a day?**
- Positive screen is response greater than 0 or when the patient is having difficulty coming up with the correct number.
 - 82% sensitive for unhealthy alcohol use
 - 79% specific for unhealthy alcohol use

Smith PC et al. J Gen Intern Med 2009; McNeely J et al. J Gen Intern Med 2015; 30:1757.



Screening for AUD in the Clinical Setting

AUDIT-C

Please circle the answer that is correct for you.

1. How often do you have a drink containing alcohol?					SCORE
Never (0)	Monthly or less (1)	Two to four times a month (2)	Two to three times per week (3)	Four or more times a week (4)	_____
2. How many drinks containing alcohol do you have on a typical day when you are drinking?					
1 or 2 (0)	3 or 4 (1)	5 or 6 (2)	7 to 9 (3)	10 or more (4)	_____
3. How often do you have six or more drinks on one occasion?					
Never (0)	Less than Monthly (1)	Monthly (2)	Two to three times per week (3)	Four or more times a week (4)	_____
TOTAL SCORE					
Add the number for each question to get your total score.					_____

Maximum score is 12. A score of ≥ 4 identifies 86% of men who report drinking above recommended levels or meets criteria for alcohol use disorders. A score of > 2 identifies 84% of women who report hazardous drinking or alcohol use disorders.

Bush K. et al 1998. The AUDIT alcohol consumption questions (AUDIT-C): an effective brief screening test for problem drinking. Arch. Intern. Med.






Medications to Treat AUD




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FDA Approved Medication	Dosage	Pharmacologic target
Naltrexone	PO: 50mg q day IM: 380 mg Q monthly	<ul style="list-style-type: none"> - Antagonism of Mu Opioid receptors - Decreases dopamine release in the nucleus <u>accumbens</u> - Decreases reward and cravings
<u>Acamprosate</u>	666mg TID Lower doses for poor renal <u>fxn</u> or <u>wt</u> < 60kg	<ul style="list-style-type: none"> - Antagonism of NMDA glutamate receptors - Agonist at GABA receptors - Balance excitatory and inhibitory neurotransmission
<u>Disulfiram</u>	250-500mg Q day	<ul style="list-style-type: none"> - Inhibits aldehyde <u>dehydroxylase</u> and dopamine hydroxylase - Acetyl-aldehyde builds up and causes adverse reaction




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Case 1:

- 30 year old male, drinks daily, sometimes to the point of “blacking out”
- Sometimes stops cold turkey, then relapses due to ETOH cravings
- Historically, forgets to take medications
- Father has AUD

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Naltrexone

- FIRST LINE TREATMENT
- **Can be used while still drinking**
- Cannot be used in patients taking opioids for pain
- Depot formulation (Vivitrol)
 - 380 mg IM monthly
 - Improves adherence
- Clinical correlation with positive response:
 - Family history of ETOH dependence
 - Strong cravings for ETOH
- Multiple analysis show small to moderate effects on reduced alcohol consumption compared to placebo
- Meta-analysis in 2010:
 - 50 randomized trials
 - N=7793
 - Reduced risk of drinking to 83% of risk seen in placebo
 - Reduced drinking days by ~ 4%
 - Particular benefit in OPRM1 polymorphism (Asp variant)
 - Less likely to relapse
 - 6 times more likely to have favorable outcome

Rosner S et al. Cochrane Database Syst Rev. 2010

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Case 2

- 38 year old female just out of 28 day inpatient AUD rehab
- Heavy daily drinker x 10 years, has Hepatitis C
- Worried about relapsing once she “goes back to the real world”

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Acamprosate

- Multiple meta-analysis show reduced alcohol consumption vs. placebo
 - Reduced relapse
 - Increased cumulative abstinence
 - Metabolized by kidneys
 - **Better for abstinence maintenance vs. reduction of alcohol use**
- Subsequent trials in US and Australia did not find statistical benefit
 - European trials had higher AUD severity in less controlled environment
 - COMBINE study required > 4 days and < 21 days abstinent

Swift RM, Aston ER. *Harvard review of psychiatry*. 2015

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Case 3

- Highly respected 55 year old Judge
- “Sneak drinker” for years until started having occupational problems
- At risk of losing law license, now has court mandated treatment and monitoring
- Has supportive but worry wife who is having trouble trusting him

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Disulfiram

- SECOND LINE TREATMENT
- Requires abstinence prior initiation
- Overall, evidence is mixed
 - Some trials no better than placebo
 - In 605 veterans, reduced drinking days
 - High rate of non-compliance
- Effective when taken routinely under supervised conditions
 - N=243
 - Regular supervision over 12 weeks
 - randomly assigned to Disulfiram, Naltrexone, Acamprosate
 - Disulfiram group:
 - Greater reduction in heavy drinking days and average weekly consumption
 - Longer time to first drink
 - Benefits diminished in unsupervised treatment period of up to 52 weeks

Fuller RK, et al. JAMA. 1986. Laaksonen E et al. Alcohol. 2008

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FDA Approved Medication Summary:

- Naltrexone has most evidence of clear treatment benefit
 - Can be started while still drinking
- Acamprosate is first line of FDA approved medications in Hep C/ liver disease due to lack of liver metabolism
 - Better to maintain abstinence
- Disulfiram should generally be avoided, though evidence supports use in select cases
 - Most effective when closely monitored
 - Liver toxicity can be fatal

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NON-FDA Approved Medication	Dosage	Pharmacologic target
Baclofen	10mg TID- ? 90 mg TID	GABA _B Receptor agonist
Gabapentin	100mg-900mg TID	Inhibits excitatory voltage gated Calcium ion channels Stimulates inhibitory GABA _B receptors
Ondansetron	1-16 µg/kg BID	5HT ₃ Antagonist
Topiramate	75mg daily- 150 mg BID	Antagonizes glutamate receptors --facilitates GABA _A
Varenicline	1mg BID	Nicotinic Acetylcholine Receptor partial agonist/agonist
Sertraline	200mg daily	Selective serotonin reuptake inhibitor

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Case 4

- 32 year old female with anxiety and insomnia, has mild alcohol withdrawal symptoms.
- Drinking “helps me calm down and is the only way I can get any sleep”
- Trigger for drinking is anxiety and insomnia

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Gabapentin

- No Hepatic metabolism, can be used to minimize ETOH withdrawal
- A randomized controlled trial showed reduction in ETOH use, decreased cravings and improved sleep
 - N=150
 - treatment with 900mg or 1800mg daily vs placebo
 - 1800mg daily more effective than 900mg daily
- A study comparing placebo to naltrexone versus naltrexone + gabapentin found **additive effects and improved sleep in combo group**

Mason BJ et al. JAMA. 2014
Anton RF et al. Am J Psychiatry. 2011

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Case 5

- 40 year old female with AUD, trauma history, insomnia
- Wants to stop drinking for her kids but “obsesses” about drinking, especially in the evenings, and “gives in” right when her kids go to sleep
- If she does not drink, feels anxious, cant sleep
- Also has frequent headaches

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Topiramate

- Endorsed by the National Institute on Alcohol Abuse and Alcoholism (NIAAA) based on strong evidence for efficacy
- Numerous studies, including randomized controlled trials and a meta analysis of 3 studies (N= 691) **showed moderate but robust reduction in ETOH use:**
 - Decreased number of drinks per day
 - Decreased number of drinking days
 - Increase in abstinence
- **May have better benefit in patients with typology of craving characterized by drinking obsessions and automaticity of drinking**

Jonas DE et al. JAMA. 2014

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Non FDA Medication Summary

- Gabapentin has moderate effects, can be used in ETOH withdrawal
 - More effective at higher dose of 1800mg daily
 - Reduces anxiety
 - Improves sleep
 - Additive effects when used with naltrexone
 - Has some abuse potential

- Topiramate has robust moderate effects on decreasing heavy drinking
 - May be best for people with drinking obsessions and automaticity of drinking
 - Can cause cognitive/memory side effects
 - May improve sleep

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Alcohol Withdrawal Can be Life Threatening

- Important to assess for risk factors for complicated withdrawal:
 - Age
 - Comorbidities
 - Head trauma
 - Frequency of use
 - Amount consumed
 - Higher BAC
 - History of complicated withdrawal

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Signs and Symptoms of Alcohol Withdrawal

Table 1. Clinical Manifestations of Alcohol Withdrawal^a

Phase/Symptoms	Onset after last drink	Duration
Early Withdrawal Tremulousness Anxiety Palpitations Nausea Anorexia	6-8 h	1-2 d
Withdrawal Seizures Tonic-Clonic Seizures	6-48 h	2-3 d
Alcoholic Hallucinosis Hallucinations Visual Tactile Auditory	12-48 h	1-2 d
Delirium Tremens Tachycardia Hypertension Low-grade fever Diaphoresis Delirium Agitation	48-96h	1-5 d

^ah=hours, d=days
Reprinted with permission from *N Engl J Med*. Management of drug and alcohol withdrawal. 2003;348:1786.

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Alcohol Withdrawal Delirium

- 3-5% of patients hospitalized with AWS
 - Onset 3-14 days after onset of AWS
 - Lasts 8 days or more
- Altered sensorium!
 - Delirium, disorientation, global confusion
 - Fever, autonomic hyperactivity, hallucinations
agitation/somnolence
- Mortality: 1-4%
 - Hyperthermia, arrhythmia, complications of seizures,
metabolic/electrolyte, and infectious complications

Schuckit, NEJM, 2014

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Clinical Institute Withdrawal Assessment of Alcohol Scale (CIWA)

- 10-item scale that objectively assesses the development and severity of withdrawal
 - Nausea and vomiting
 - Tremor
 - Paroxysmal sweats
 - Anxiety
 - Agitation
 - Auditory disturbances
 - Visual disturbances
 - Headache
 - Orientation
- Serves as a basis for prescribing medication management

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THANK YOU!

QUESTIONS?

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- www.cdc.gov. National Center for Chronic Disease Prevention and Health Promotion, Division of Population Health, Alcohol and Public Health
- www.cdc.gov. Early release of selected estimates based on data from the 2017 National Health Interview Survey

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Knowledge Check Question 1

In the United States, a standard drink:

- A) is a glass of wine or can of beer.
- B) **contains ~ 14 grams of pure alcohol.**
- C) is anything containing alcohol.
- D) is at least 8 oz.

Rationale for correct answer: That is correct! A standard drink contains 14 grams of pure alcohol, regardless of the volume of the beverage. Different types of beer, wine or liquor can have very different amounts of alcohol content

Rationale for incorrect answer: That is incorrect. A standard drink contains 14 grams of pure alcohol, regardless of the volume of the beverage. Different types of beer, wine or liquor can have very different amounts of alcohol content

Reference: <https://www.niaaa.nih.gov/alcohol-effects-health/overview-alcohol-consumption/what-standard-drink>

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Knowledge Check Question 2

Alcohol use disorder is a problematic pattern of alcohol use leading to clinically significant impairment or distress. What is the minimum number out of the 11 DSM-5 criteria that must be met for a person to be diagnosed with Alcohol Use disorder?

- A) 1
- B) **2**
- C) 4
- D) 6

Rationale for correct answer: That is correct! Alcohol use disorder can be diagnosed if a person has at least 2 of 11 criteria identified as problematic by the DSM-5

Rationale for incorrect answer: That is incorrect. Alcohol use disorder can be diagnosed if a person has at least 2 of 11 criteria identified as problematic by the DSM-5

Reference: American Psychiatric Association (2013). Diagnostic and Statistical Manual of Mental Disorders (Fifth ed.). Arlington, VA: American Psychiatric Publishing

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Knowledge Check Question 3

Which of the following is true about increasing the risk of developing alcohol use disorder?

- A) **onset of alcohol use prior age 15**
- B) being of Hispanic race
- C) being female rather than male
- D) being the only person in the family that uses alcohol

Rationale for correct answer: That is correct! Individuals who start drinking prior age 15 are 4 times more likely to develop alcohol dependence

Rationale for incorrect answer: That is incorrect. Individuals who start drinking prior age 15 are 4 times more likely to develop alcohol dependence. Those of Native American and Caucasian descent are more likely to develop AUD than Hispanic or Black individuals. Males are more likely to have AUD compared to females.

Reference: www.cdc.gov, National Center for Chronic Disease Prevention and Health Promotion, Division of Population Health, Alcohol and Public Health

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Knowledge Check Question 4

- Which of the following is true about Naltrexone?
 - A) It can be used in patients taking opioids for pain
 - B) It can be used even if the patient is still drinking
 - C) It only comes in pill form and cannot be injected
 - D) It is a second line treatment for AUD

Rationale for correct answer: That is correct! Individuals can use naltrexone while still drinking.

Rationale for incorrect answer: That is incorrect. Individuals can use naltrexone while still drinking. They cannot use naltrexone if taking opioids for pain. It is a first line treatment for AUD and can be taken orally or in a depot formulation given IM monthly.

Reference: Rosner S, Hackl-Herrwerth A, Leucht S, et al. Opioid antagonists for alcohol dependence. *Cochrane Database Syst Rev* 2010; CD001867

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Knowledge Check Question 5

- Which of the following is true about Acamprosate?
 - A) It is metabolized by the liver
 - B) It is metabolized by the kidneys
 - C) It is taken once a day
 - D) It can be given as a monthly shot

Rationale for correct answer: That is correct! Acamprosate is metabolized by the kidneys.

Rationale for incorrect answer: That is incorrect. Acamprosate is metabolized by the kidneys. It is taken three times a day and is only available in an oral formulation

References: Swift RM, Aston ER. Pharmacotherapy for Alcohol Use Disorder: Current and Emerging Therapies. *Harvard review of psychiatry*. 2015;23(2):122-133. doi:10.1097/HRP.0000000000000079.

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Knowledge Check Question 6

Alcohol withdrawal is

- A) uncomfortable but not life threatening
- **B) possibly life threatening**
- C) always accompanied by seizures
- D) inevitable in people who drink daily

Rationale for correct answer: That is correct! Alcohol withdrawal is possibly life threatening

Rationale for incorrect answer: That is incorrect. Alcohol withdrawal is possibly life threatening.

Reference: ASAM National Practice Guideline on Alcohol Withdrawal Management, 2020