ASAM American Society *of* Addiction Medicine

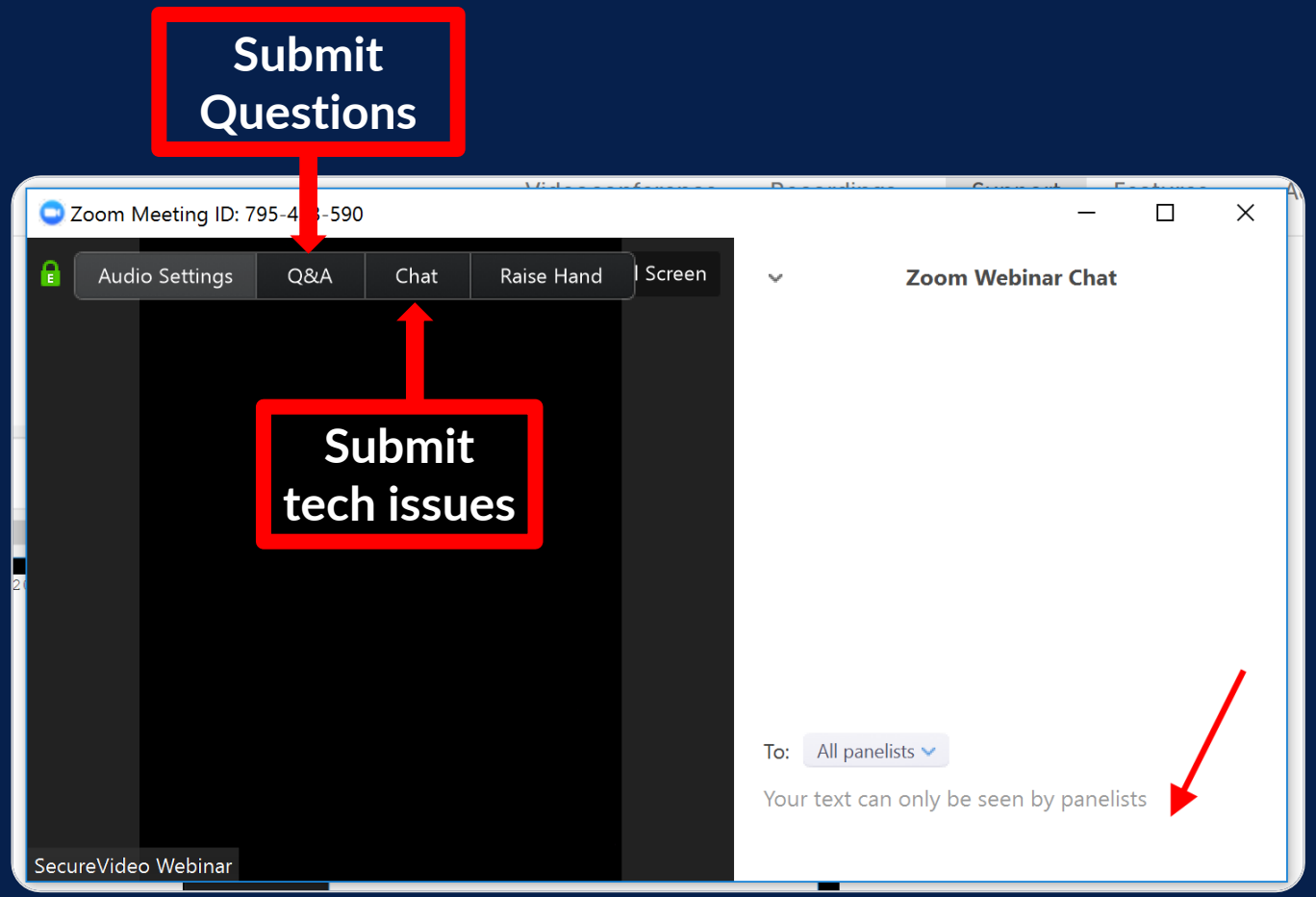
THE ASAM 2020 CLINICAL PRACTICE GUIDELINE ON ALCOHOL WITHDRAWAL MANAGEMENT:

Pharmacotherapy

SCHEDULE

1:00 - 1:05 pm	Announcements ASAM STAFF
1:05 - 1:45 pm	Presentation Dr. Weaver
1:45 - 2:00 pm	Q&A Session Dr. Weaver
2:00 pm	Closing Remarks ASAM STAFF

ANNOUNCEMENTS



1. **Attendee Audio:** Your mics are automatically set to mute.
2. **Questions?** Type questions into the Q&A box.
3. **Technical Issues?** Use the chat box feature to submit questions to your hosts.

HOW TO CLAIM CME

1. **Go to:** https://elearning.asam.org/p/AWM2020_Webinar4
2. **Go to:** *Contents* tab
3. **Complete:**
   - ☑ CME Quiz
   - ☑ Evaluation
   - ☑ Credit and Certificate

PRESENTER

Michael Weaver, MD, DFASAM

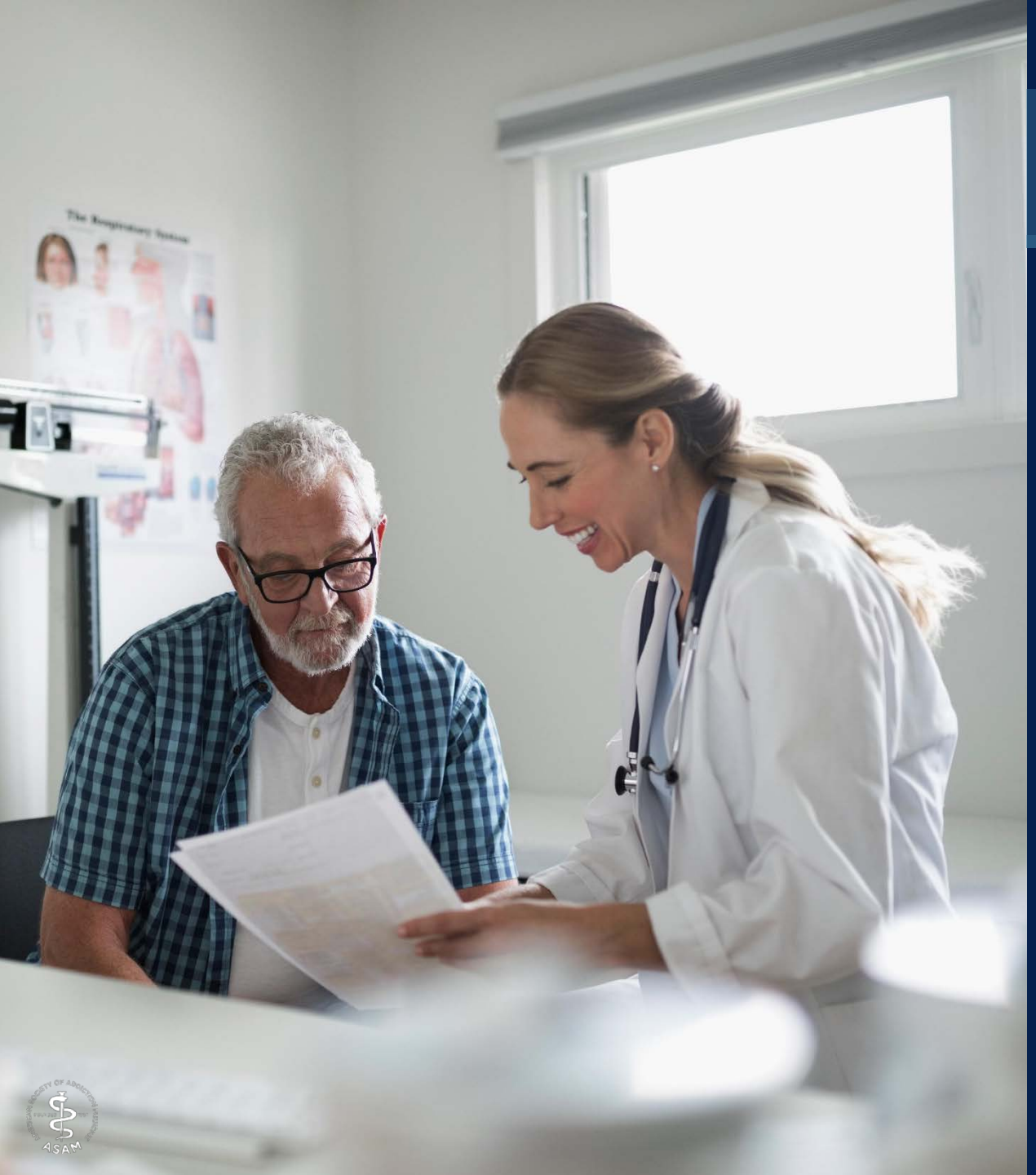
- Michael Weaver, MD, DFASAM is a Professor in the Department of Psychiatry and Medical Director of the Center for Neurobehavioral Research on Addictions (CNRA) at the McGovern Medical School at the University of Texas Health Science Center at Houston.

- Dr. Weaver has been a member of ASAM for over 20 years and currently serves as a member of the Publications Council and the Annual Conference Program Planning Committee. He is currently involved in patient care, medical education, and research. He sees patients in the Innovations Addiction Treatment Clinic at the Texas Medical Center in Houston.

- He has extensive experience teaching about addiction to medical students, residents, and community professionals at all levels. Dr. Weaver has multiple publications in the field of addiction medicine, including the book "Addiction Treatment" published by Carlat Publishing in 2017.

Disclosure Information

- Carlat Publishing
- American Board of Preventive Medicine



LEARNING OBJECTIVES

At the end of this webinar, you will be able to:

1. Summarize the guideline's treatment recommendations around pharmacotherapy and discuss how they should be used in practice.
2. Recognize all medications that can be used to treat patients with alcohol withdrawal and explain the circumstances in which one form of medication can be more effective than another.
3. Understand the limitations and risks associated with the various medications used to treat patients with alcohol withdrawal.

Pharmacotherapy

CASE 1

- 38 y/o male admitted to the hospital with **multilobar pneumonia**
- Initial VS: **BP 130/85, HR 90, RR 14, T 98.6°F**
- He drinks “some beer most days”
- Shortly after being admitted, he becomes anxious, spills water when he tries to drink it from the cup
- Later that night, **BP is 150/90, HR 115, T 100.3°F**
- He sees Uncle Alfred in the room and complains that there is a spider in his bed

CASE 1

Which of the following medications do you give this patient now?

A. Acamprosate

B. Chlordiazepoxide

C. Clonidine

D. Haloperidol

CASE 1

Answer:

B. Chlordiazepoxide

The only medicine listed that is cross-tolerant with alcohol.

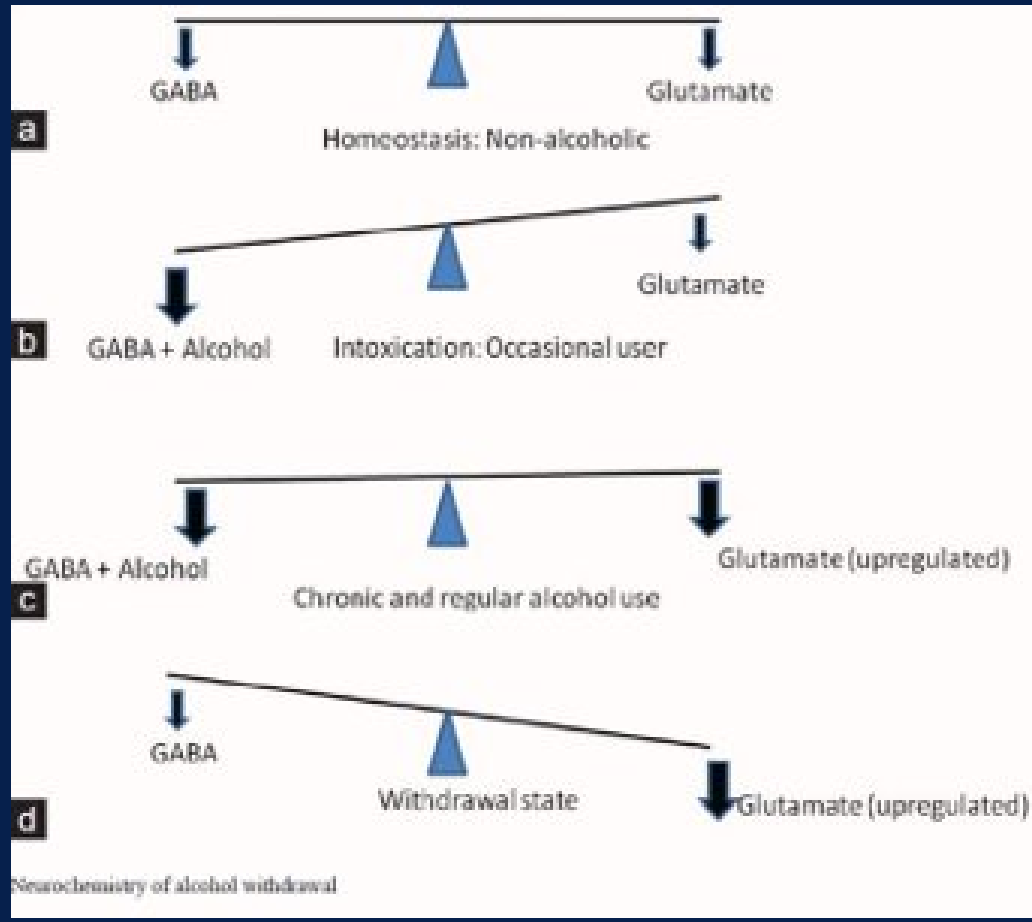
Benzodiazepines are first-line treatment for alcohol withdrawal syndrome.

ALCOHOL WITHDRAWAL SYNDROME (AWS) MEDICATION CONSIDERATIONS

1. Need to prevent serious, life-threatening signs and symptoms
2. Need to ameliorate current **signs and symptoms**, prevent return to alcohol use
3. Side effect and safety profiles
4. Available **routes of administration** (PO, IM, IV)

MEDICATIONS USED FOR AWS MONOTHERAPY

- Targets the GABA and/or glutamate system
- Benzodiazepines
- Phenobarbital
- GABA sensitive anticonvulsants



Neurochemistry of alcohol withdrawal

BENZODIAZEPINES (BZDs)

Indications

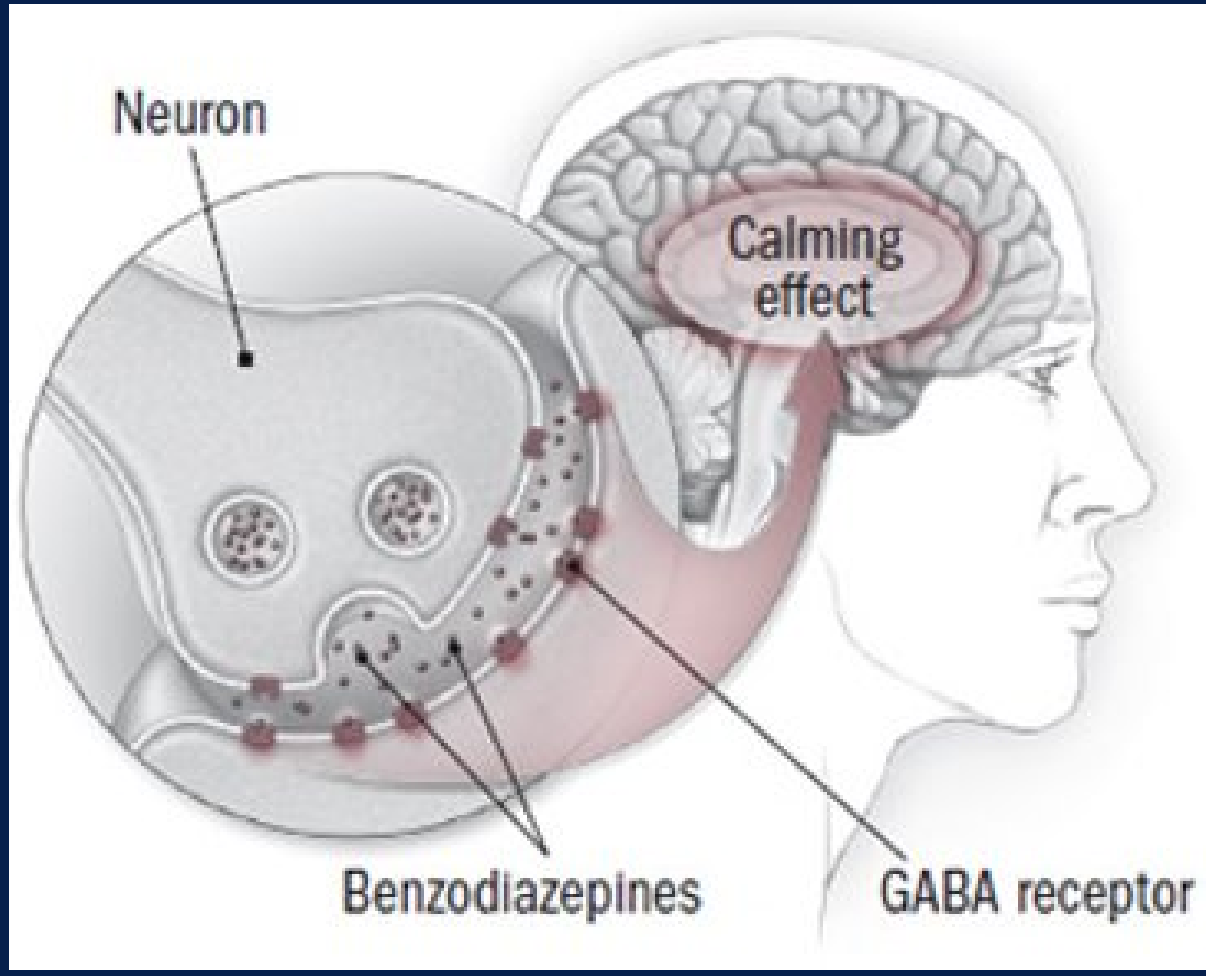
- Acute or generalized anxiety
- Insomnia
- Seizures

A few examples:

- Midazolam (short-acting)
- Temazepam (short-acting)
- Lorazepam (intermediate)
- Chlordiazepoxide (long-acting)
- Diazepam (long-acting)
- Clonazepam (long-acting)

HOW BENZODIAZPINES WORK

- Facilitate **inhibitory effects** of gamma-aminobutyric acid (GABA) receptor complex
- Non-selective binding to benzodiazepine (BZ) receptors
- Effects similar to **alcohol**
  - Intoxication
  - Withdrawal
- **Cross-tolerant** with alcohol



BENZODIAZEPINES FOR AWS

BZDs are appropriate for:

- Most patients
- In all settings

Preferred for:

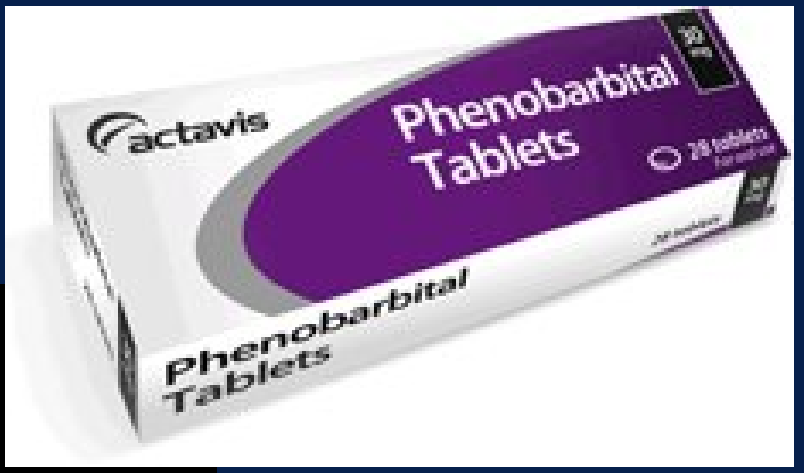
- Prophylaxis
- Severe Alcohol Withdrawal Syndrome
- Seizure
- Alcohol Withdrawal Delirium

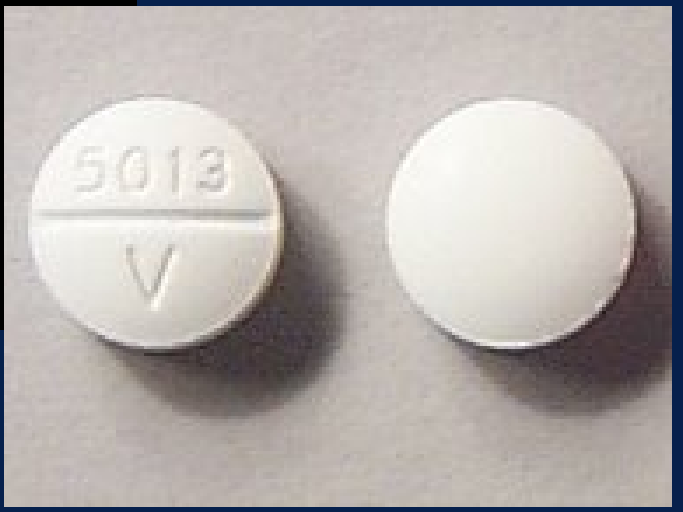
Because:

- Most empirical evidence of efficacy and safety
- Well-documented effectiveness in reducing the signs and symptoms of AWS and the incidence of seizure and alcohol withdrawal delirium
- However, risk of over-sedation and respiratory depression

PHENOBARBITAL (PHB)

- Long half-life of **up to 7 days**
- No significant euphoria
  - Not usually diverted
  - Unlike benzodiazepines
- Oral tablets or liquid, or parenteral forms
- Safe in **liver and kidney disease**
  - 30% excreted unchanged in urine
- Inexpensive when compared to alternatives





PHENOBARBITAL

PHB is appropriate for:

- Prophylaxis
- Severe or complicated AWS

Especially if:

- BZDs contraindicated
- Patient not responding to BZDs

But only if:

- Clinicians have training and experience using it for AWS
- Patients are observed (not Level 1-WM)

Because:

- No evidence of better efficacy than BZDs
- More side effects than BZDs
- Relatively narrow therapeutic window and long half-life (up to 7 days) make PHB difficult to dose accurately without significant training
- Is the next best alternative to BZDs for severe and complicated AWS
- Acts on GABA and glutamate signaling. BZDs only augment GABA.

ANTICONVULSANTS: CARBAMAZEPINE (CBZ) AND GABAPENTIN (GBP)

CBZ and GBP are appropriate for:

- Mild or moderate AWS

Especially if:

- BZDs contraindicated
- Plan to use GBP for ongoing Alcohol Use Disorder (AUD) treatment

Because:

- Sufficient evidence of efficacy and safety for mild to moderate AWS
- Compared to BZDs and PHB
  - Better safety profile
  - Less sedating
  - Lower risk of drug-drug interaction
- Not enough evidence for treating AWS-related seizure or AWD

ALPHA2-ADRENERGIC AGONISTS (A2AAs) AND BETA-ADRENERGIC ANTAGONISTS (BETA-BLOCKERS)

A2AAs and Beta-Blockers are appropriate for:

- Only as an adjunct to BZDs

A2AAs

- Autonomic hyperactivity and anxiety

Beta-Blockers

- Persistent hypertension or tachycardia

Because:

- They reduce the signs of sympathetic activation
- They do not treat the underlying syndrome
- They may mask signs of worsening syndrome

DEXMEDETOMIDINE AND PROPOFOL

Dexmedetomidine and Propofol are appropriate for:

- As an adjunct to BZDs
- For patients with AWS or Resistant Alcohol Withdrawal (RAW) being treated in the ICU and who already require intubation

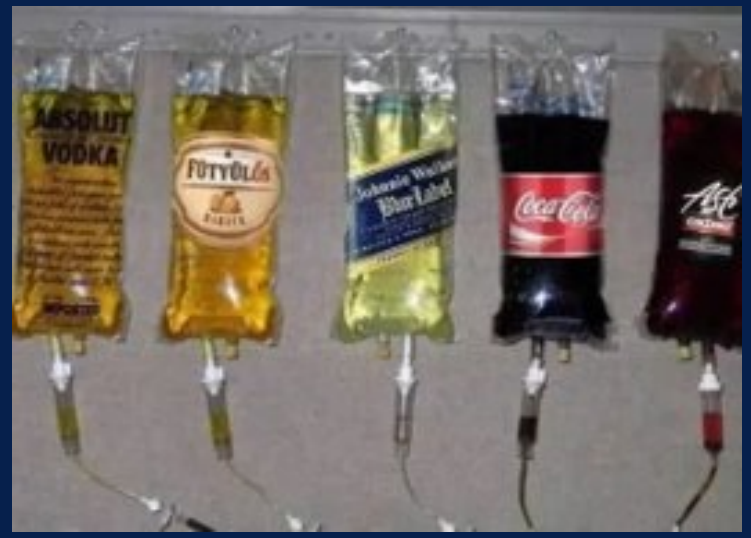
Because:

- They can reduce the agitation and delirium associated with AWS and RAW through sedation
- They do not treat the underlying syndrome

DO NOT USE

To prevent or treat AWS:

- Alcohol
- Baclofen
- Magnesium (to treat AWS)

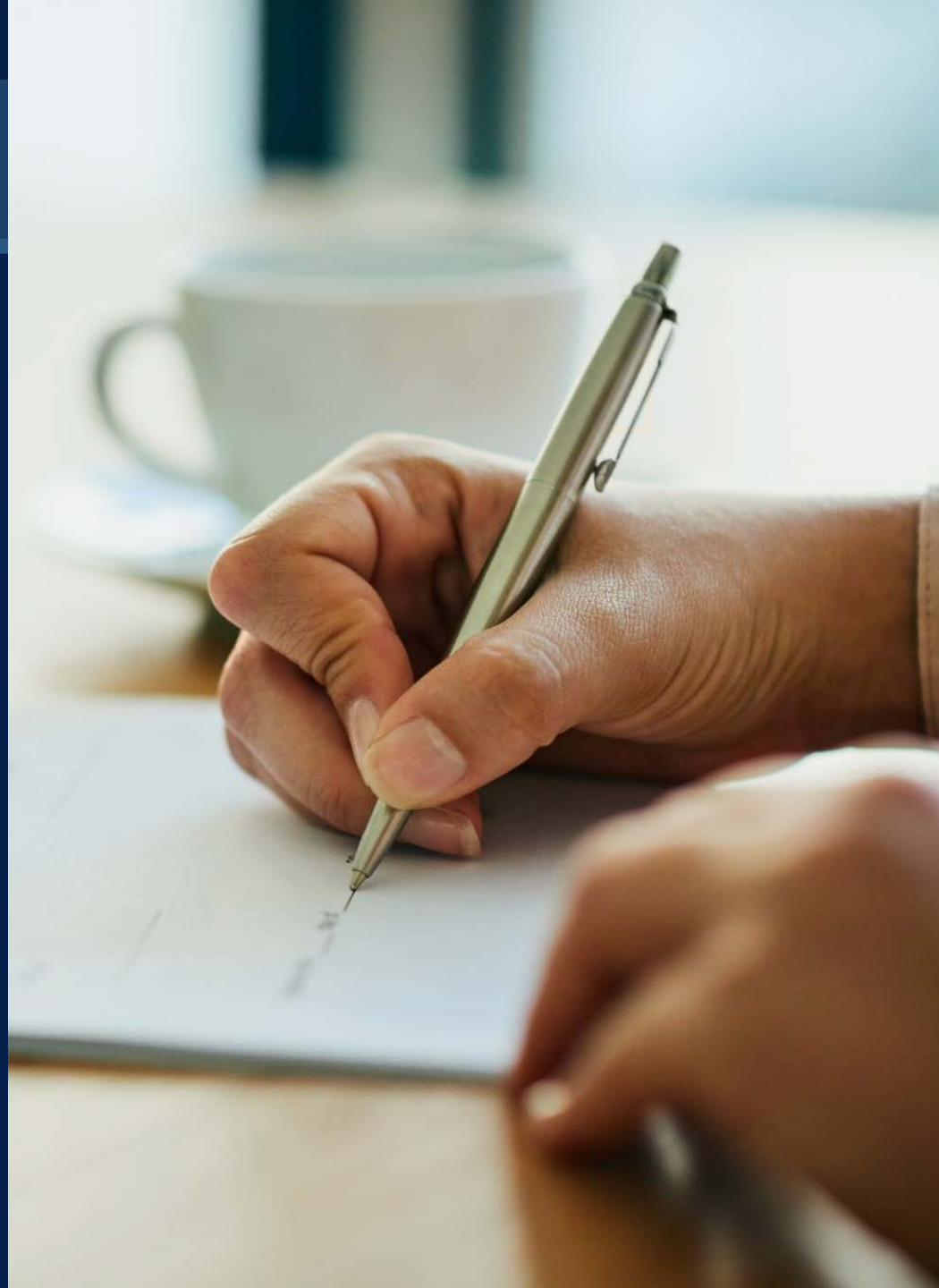


Because:

- Administration of oral or intravenous alcohol has no proven efficacy and known toxicity
- There's not enough evidence yet for baclofen
- There is evidence magnesium is not effective at treating AWS signs and symptoms

CASE 2

- 46 y/o woman has been drinking 4-5 glasses of wine **daily** for the past 6 months
- She is prescribed **alprazolam (Xanax) 1 mg 3 times daily** for Generalized Anxiety Disorder by her Primary Care Physician
- She is arrested for driving on a suspended license and incarcerated over the weekend
- After her second day of incarceration, she develops a **tremor** in both hands, is diaphoretic, anxious, and keeps swatting at flies that no one else can see



CASE 2

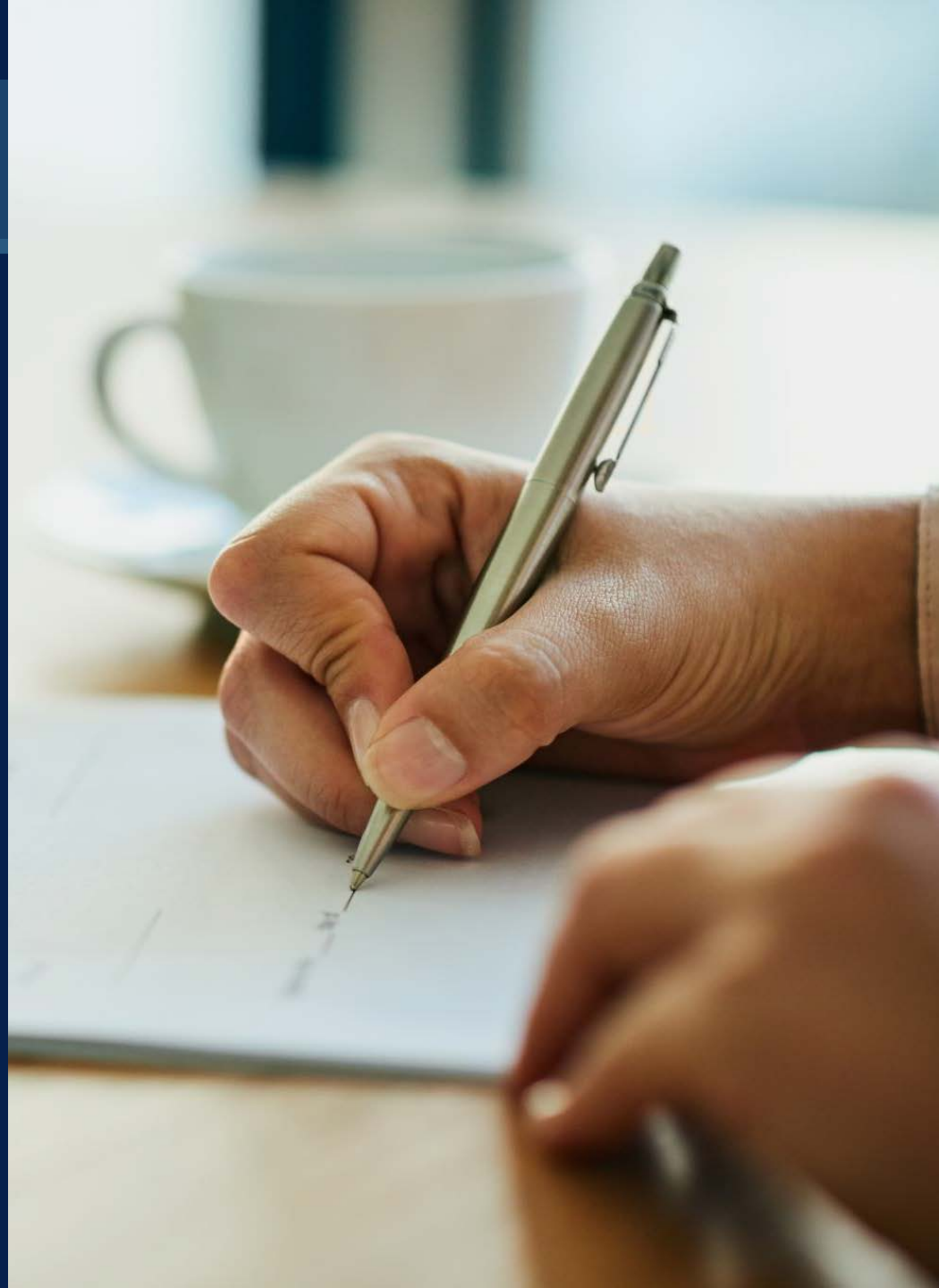
Which of the following medications is most appropriate to administer to this patient now?

A. Alprazolam

B. Phenobarbital

C. Risperidone

D. Thiamine



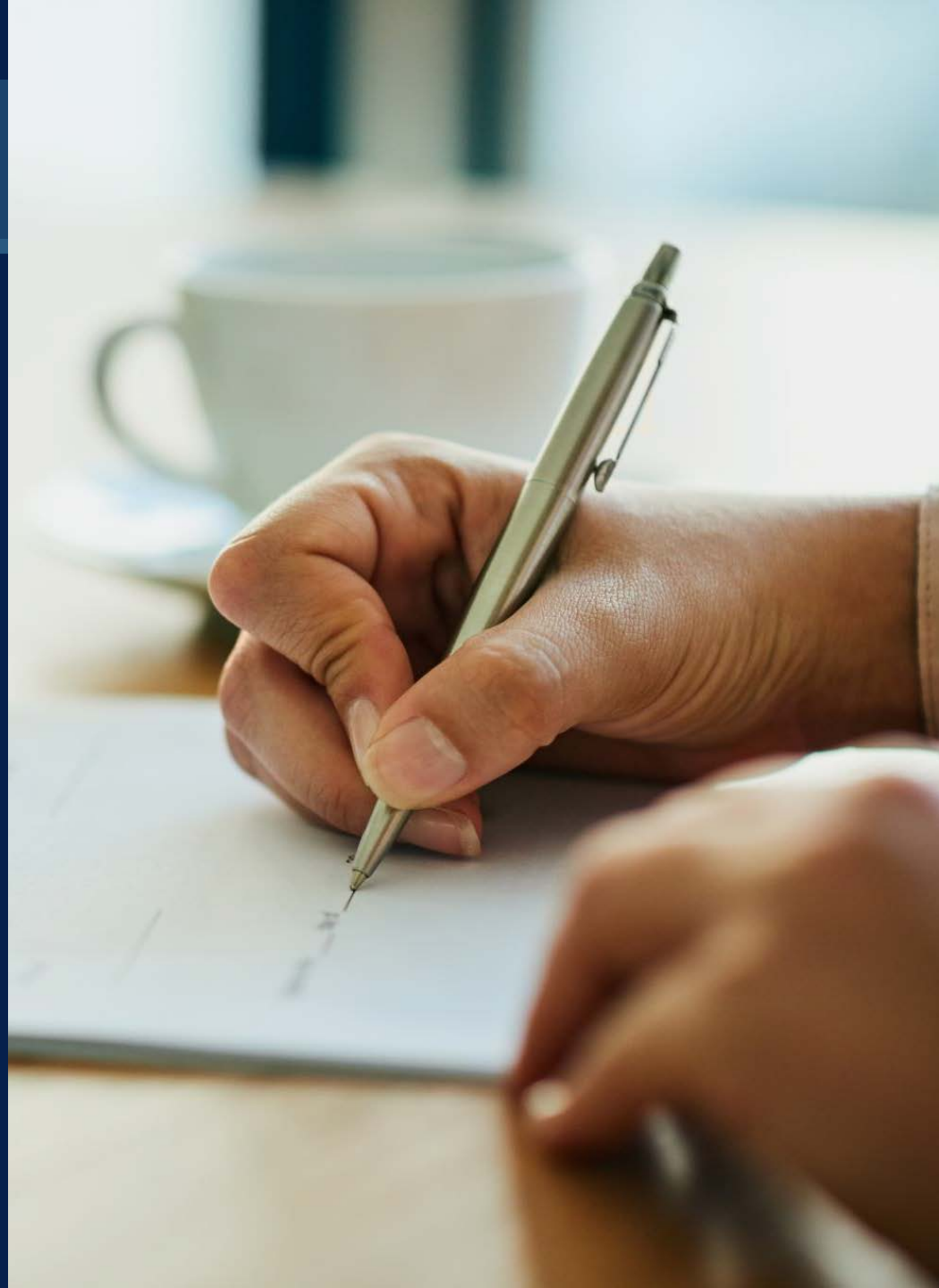
CASE 2

Answer:

B. Phenobarbital

It is cross-tolerant with alcohol, long-acting, and not being used by the patient.

Phenobarbital should be used by clinicians experienced with its use in settings that offer close monitoring.



AWS PREVENTION

- Patients at risk of developing **severe, complicated, or complications of AWS** should get preventative medication regardless of their current signs and symptoms.
- In ambulatory settings, **patients at risk of worsening AWS** should also get preventative take-home medication.

Rationale

- Signs and symptoms can escalate quickly
- Medication can prevent the development of life-threatening signs and symptoms
- In ambulatory AWS management, signs and symptoms might develop while a patient is away from the treatment setting
- Patients with even very mild AWS will benefit from some take-home doses

TREATING CURRENT SIGNS AND SYMPTOMS

- Patients with **mild AWS** who are not at risk of developing worse symptoms can be treated with supportive care alone OR with medication
- Patients with **at least moderate severity AWS** should be treated with medication

Rationale

- Mild signs and symptoms can be safely and effectively managed with supportive care
- However, minimizing signs and symptoms reduces the likelihood of a return to alcohol use. Untreated withdrawal may also contribute to the kindling effect.
- Moderate AWS at treatment baseline is a risk factor for developing more severe signs and symptoms

MONITORING TREATMENT RESPONSE

If symptoms are not controlled as expected:

- Consider increasing the dose
- Reassess for **appropriate LOC**
- Consider switching medications
- If using a BZD, consider adding an **adjunct medication**

Rationale

- Patients with AWS may require larger doses than typically seen in other patient populations, particularly in the case of early severe withdrawal
- Failure to respond may reflect:
  - More severe withdrawal than expected and significant risk of major complications
  - Withdrawal from another GABAergic agent
  - BZD resistance as seen in kindling

BENZODIAZPINES FOR AWS

- Longer-acting BZDs are **preferred**
- Discontinue a BZD prescription for AWS following treatment

Rationale

- Longer-acting BZDs are not more effective, but the clinical benefit from longer duration of action contributes to a smoother course of withdrawal and greater control of breakthrough and rebound signs and symptoms
- Any BZD use has an associated risk of dependence

BENZODIAZPINE COMPLICATIONS

- Monitor patients taking BZDs for signs of **over-sedation and respiratory depression**
- More likely with:
  - High doses
  - Older age
  - Impaired hepatic function
- If liver disease is suspected, **do not delay treatment**. Use a BZD with less hepatic metabolization

Rationale

- BZD metabolites can accumulate and lead to over-sedation and respiratory depression
- This is more likely when longer-acting agents are used in high doses, in older patients, and those with impaired hepatic function.
- It is important to recognize complications of BZD use early to intervene in a timely manner

BENZODIAZPINE ADJUNCT MEDICATIONS

High risk of severe, complicated, or complications of AWS

- PHB (in highly supervised settings)

Moderate AWS

- CBZ, GBP, VPA (liver, childbearing)

Severe AWS

- CBZ, GBP, VPA (liver, childbearing)
- PHB (in highly supervised settings)

AWD or Resistant Alcohol Withdrawal

- PHB, Dexmedetomidine, Propofol

Persistent hypertension, tachycardia, anxiety

- A2AAs, Beta-Blockers

Rationale

- Some patients benefit from additional medication to manage signs and symptoms not controlled by BZDs alone
- Anticonvulsants target GABA in a different way than BZDs
- PHB acts on GABA as well as glutamate signaling. It is synergistic with BZDs and this combination increases risk of over sedation and respiratory depression
- Some patients need specific AWS signs targeted

CASE 3

- 27 y/o man is hospitalized for **surgical reduction of a leg fracture** after a motor vehicle accident
- He had been driving drunk and has a couple of shots of liquor nearly **every day**
- He is monitored closely for signs and symptoms of alcohol withdrawal syndrome with a scoring scale administered every few hours
- Doses of **chlordiazepoxide** are given according to the score each time
- No dose is given if his score is not high enough

CASE 3

Which of the following best describes this type of regiment for management of alcohol withdrawal syndrome?

A. Fixed-schedule therapy

B. Front-loading

C. Sinclair method

D. Symptom-triggered therapy

CASE 3

Answer:

D. Symptom-triggered therapy

Giving medication based on severity of alcohol withdrawal symptoms using a scoring scale.

EXAMPLES: BZD DOSING REGIMENS

- Fixed Dosing
- Symptom-Triggered Dosing
- Front Loading

FIXED DOSING

What it is:

- Medication administered at **fixed intervals** according to a schedule
- Reducing the dose and/or increasing the interval creates gradual taper
- Typical taper is **3-5 days**
- Provide additional medication as needed

Benefits

- Simple
- Don't need to use a scale

Drawbacks

- Over- or underestimating dose may lead to **insufficient symptom control and over-sedation**
- Does not eliminate the need for frequent monitoring and dose adjustment

SYMPTOM-TRIGGERED DOSING

What it is:

- Medication administered only when patients are experiencing **significant signs and symptoms** according to a severity scale
  - If CIWA-Ar ≥ 10 give 25–100 mg chlordiazepoxide
- Can use score to **adjust dose**
  - If CIWA-Ar 8–15, give 15 mg oxazepam. If CIWA-Ar >15, give 30mg oxazepam
- Score also used to **determine reassessment/dosing interval**

Benefits

- Individualizes treatment according to symptom severity
- Dose is increased rapidly if needed and reduced as symptoms resolve
- Reduces risk of under- and over-treating by assessing and dosing according to real-time symptom severity

CLINICAL WITHDRAWAL ASSESSMENT

Clinical Institute Withdrawal Assessment Scale for Alcohol, Revised (CIWA-Ar)

Nausea and Vomiting
0 – No nausea or vomiting
1
2
3
4 – Intermittent nausea with dry heaves
5
6
7 – Constant nausea, frequent dry heaves and vomiting

Paroxysmal Sweats
0 – No sweat visible
1 – Barely perceptible sweating, palms moist
2
3
4 – Beads of sweat obvious on forehead
5
6
7 – Drenching sweats

Agitation
0 – Normal activity
1 – Somewhat more than normal activity
2
3
4 – Moderate fidgety and restless
5
6
7 – Paces back and forth during most of the interview or constantly thrashes about

Visual Disturbances
0 – Not present
1 – Very mild photosensitivity
2 – Mild photosensitivity
3 – Moderate photosensitivity
4 – Moderately severe visual hallucinations
5 – Severe visual hallucinations
6 – Extreme severe visual hallucinations
7 – Continuous visual hallucinations

Tremor
0 – No tremor
1 – Not visible, but can be felt at finger tips
2
3
4 – Moderate when patient's hands extended
5
6
7 – Severe, even with arms not extended

Tactile Disturbances
0 - None
1 – Very mild paraesthesias
2 – Mild paraesthesias
3 – Moderate paraesthesias
4 – Moderately severe hallucinations
5 – Severe hallucinations
6 – Extremely severe hallucinations
7 – Continuous hallucinations

Headache
0 – Not present
1 – Very mild
2 - Mild
3 - Moderate
4 – Moderately severe
5 - Severe
6 – Very severe
7 – Extremely severe

Auditory Disturbances
0 – Not present
1 – Very mild harshness or ability to frighten
2 – Mild harshness or ability to frighten
3 – Moderate harshness or ability to frighten
4 – Moderately severe hallucinations
5 – Severe hallucinations
6 – Extremely severe hallucinations
7 – Continuous hallucinations

Orientation and Clouding of the Sensorium
0 – Oriented and can do serial additions
1 – Cannot do serial additions
2 – Disoriented for date but not more than 2 calendar days
3 - Disoriented for date by more than 2 calendar days
4 – Disoriented for place/person

Cumulative scoring

Cumulative score	Approach
0 – 8	No medication needed
9 – 14	Medication is optional
15 – 20	Definitely needs medication
>20	Increased risk of complications

FRONT LOADING

What it is:

- Moderate-to-high dose of long-acting BZD given **frequently at the outset of treatment**
- Metabolism leads to natural taper
- Can be **symptom-driven**
  - 20 mg diazepam every hour while CIWA-Ar ≥10
- Or **schedule-driven**
  - 20 mg diazepam every hour for 1-2 hours or until patient is sedated

Benefits

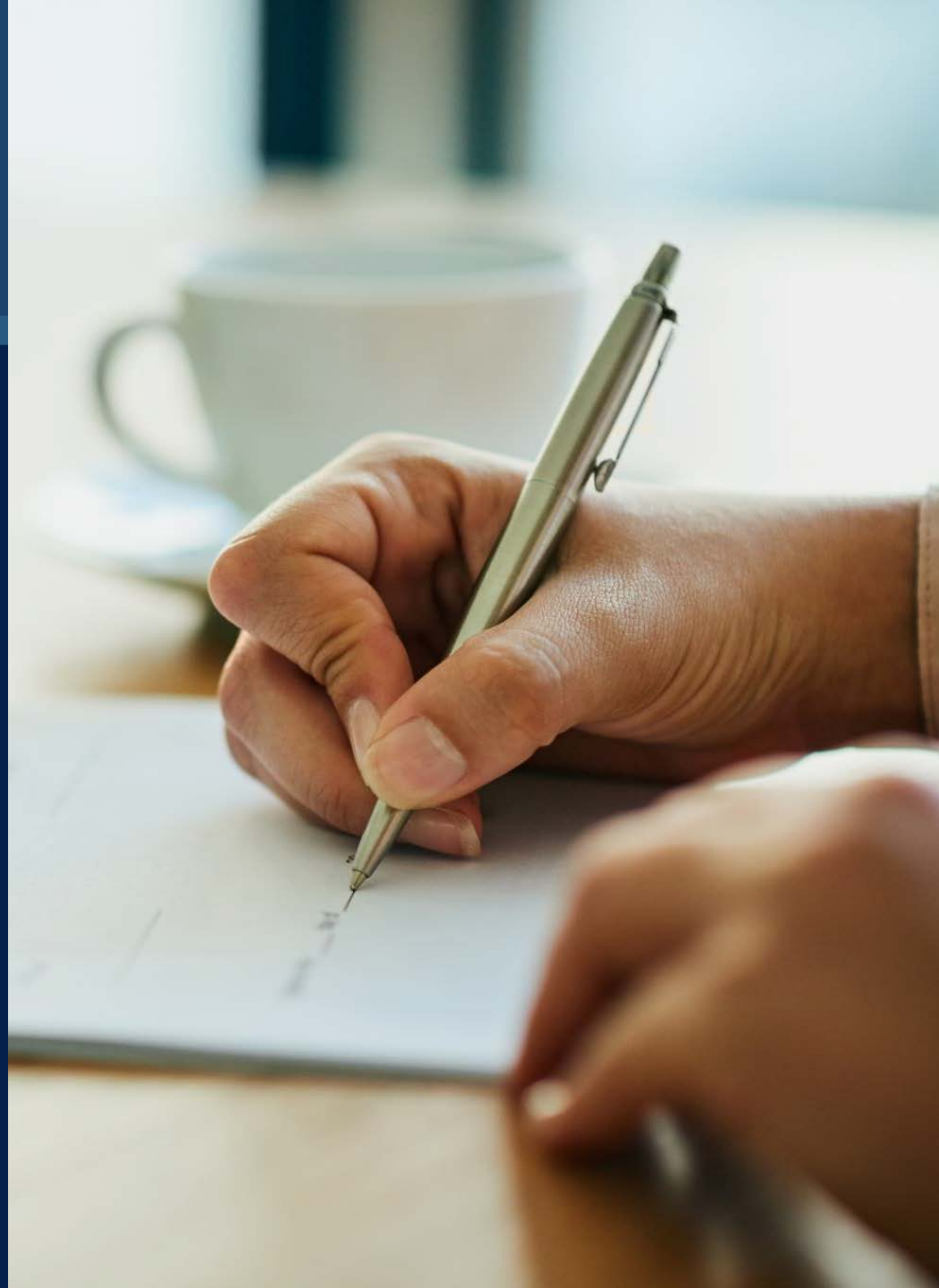
- Rapidly achieve therapeutic levels and control of AWS signs and symptoms

Drawbacks

- Can lead to over-sedation

INPATIENT SETTING

- Hospital ward or detox facility
- Alcohol withdrawal is a **life-threatening condition**
- Remove from drinking environment
- Comorbidity
  - Medical
  - Psychiatric



INPATIENT MANAGEMENT: CHOOSING A REGIMEN

- Symptom-triggered dosing is generally **preferred**
- Use fixed dosing…
  - If can't use symptom-triggered dosing
  - When using shorter-acting BZD
- If using fixed dosing, **monitor signs and symptoms** and provide additional doses as needed

Rationale

- For inpatients, symptom-triggered dosing reduces duration of treatment and length of stay compared to a fixed-dose schedule
- Levels of short-acting BZDs can diminish rapidly. Fixed dosing may be more feasible and reduce rebound and breakthrough signs and symptoms.
- Does not eliminate the need for frequent monitoring and dose adjustment

WHEN DO I CONSULT THE ICU?

- Hypotension
- Rapid **fluctuation** in vital signs
- Requiring large doses of **cross-dependent medication**
- Severe altered mental status
  - May not be able to protect airway

AUDIENCE Q & A

UPCOMING EVENTS

THE ASAM ALCOHOL WITHDRAWAL MANAGEMENT SERIES

❑ The ASAM Alcohol Withdrawal Management Webinar: Complicated Withdrawal and Special Populations	Darius Rastegar, MD, DFASAM	Tuesday, Nov. 17 @ 12:00 p.m. EST

ASAM American Society *of* Addiction Medicine

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THANK YOU.