

# One Drug to Rule Them All: Phenobarbital in Alcohol Withdrawal



UTAH SOCIETY OF  
HEALTH-SYSTEM PHARMACISTS

## Presley Whetman, PharmD

PGY1 Track A Resident  
University of Utah Health  
presley.whetman@pharm.utah.edu  
Monday March 21st, 2022

1

## Disclosures

- Relevant Financial Conflicts of Interest
  - **CE Presenter, Presley Whetman, PharmD**
    - None
  - **CE Mentor, Brianne Wolfe, PharmD, BCPS, BCCCP**
    - None
- Off-Label Uses of Medications
  - Phenobarbital for alcohol withdrawal



2

## Pharmacist Learning Objectives

- Assess a patient's overall withdrawal risk using PAWSS
- Differentiate BAWSS assessment from CIWA-Ar assessment
- Recognize possible contraindications to the use of phenobarbital
- Construct a patient-specific dosing regimen for phenobarbital in alcohol withdrawal

## Technician Learning Objectives

- Identify medications that can interact with phenobarbital on a patient's medication list
- Recognize appropriate dosage forms of phenobarbital
- Apply appropriate storage of phenobarbital formulations



3



4

## Abbreviations

- ABW – Actual body weight
- AUD – Alcohol use disorder
- AWD – Alcohol withdrawal delirium
- AWS – Alcohol withdrawal order
- BAWs – Brief Alcohol Withdrawal Scale
- BP – Blood Pressure
- BZD – Benzodiazepine
- CIWA-Ar - Clinical Institute Withdrawal Assessment for Alcohol
- DT – Delirium tremens
- ED – Emergency department
- GABA - Gamma-aminobutyric acid
- HR – Heart rate
- IBW – Ideal body weight
- ICU – Intensive care unit
- IV – Intravenous
- NMDA - N-methyl-D-aspartate
- PAWSS – Prediction of Alcohol Withdrawal Severity Scale
- PO – By mouth
- PRN – As needed
- RR – Respiratory rate
- SEWS – Severity of Ethanol Withdrawal Symptoms Score
- yo – years old



5

## Audience Response Question

Respond at [PollEv.com/ushp](https://PollEv.com/ushp)  
 ☒ Text **USHP** to **22333** once to join, then **A, B, or C**

**When treating AWS, what is your current practice most aligned with?**

- |                        |          |
|------------------------|----------|
| Benzodiazepine regimen | <b>A</b> |
| Phenobarbital regimen  | <b>B</b> |
| Mixed regimen          | <b>C</b> |



- ☒ [PollEv.com/USHP](https://PollEv.com/USHP)
- ☒ Download the Poll Everywhere app and join USHP
- ☒ Text USHP to 22333



6

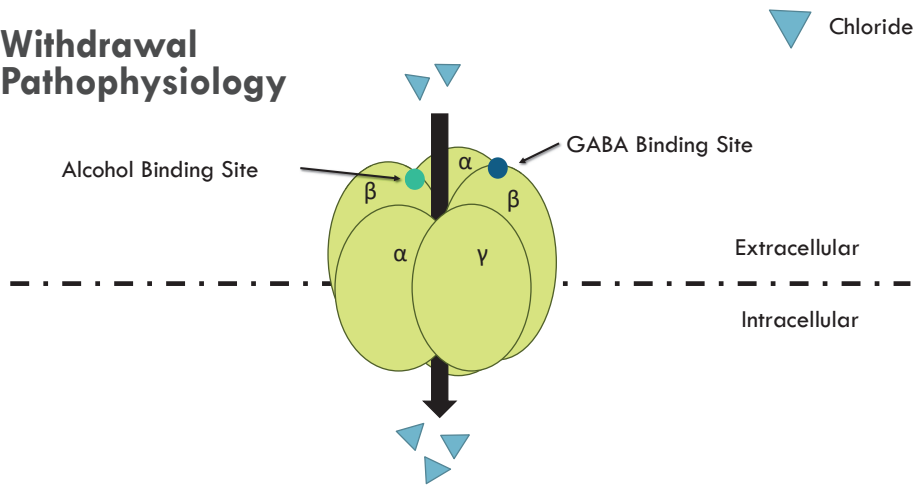
## Alcohol Use Disorder

Heavy or frequent alcohol drinking causing problems, emotional distress or physical harm

## Alcohol Withdrawal Syndrome

Imbalance in neurotransmitters in the brain caused by chronic consumption of alcohol

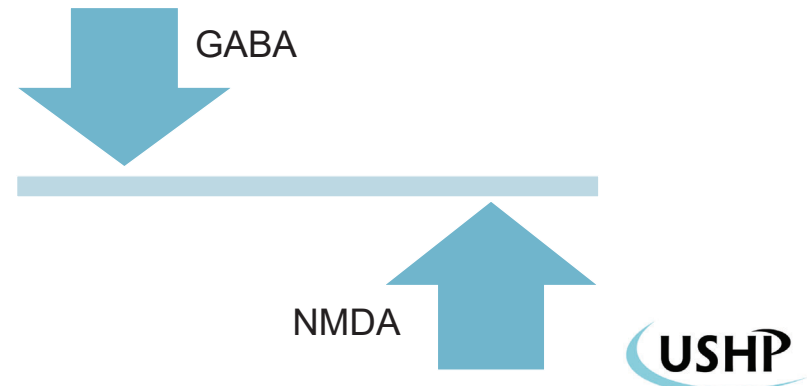
## Withdrawal Pathophysiology



Davies M. The role of GABA<sub>A</sub> receptors in mediating the effects of alcohol in the central nervous system. *J Psychiatry Neurosci*. 2003;28(4):263-274.

9

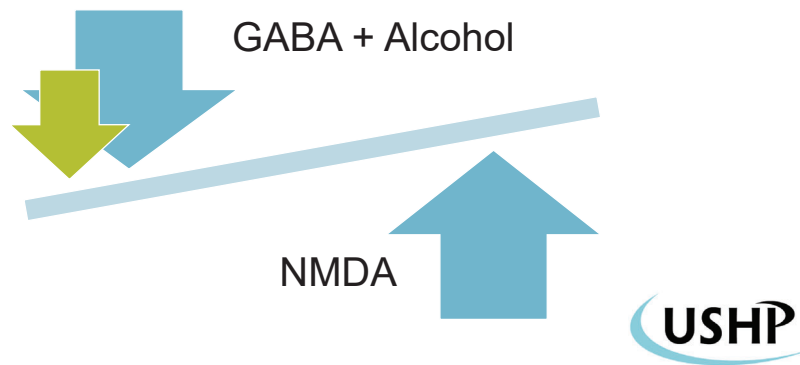
## Pathophysiology Continued



Davies M. The role of GABA<sub>A</sub> receptors in mediating the effects of alcohol in the central nervous system. *J Psychiatry Neurosci*. 2003;28(4):263-274.

10

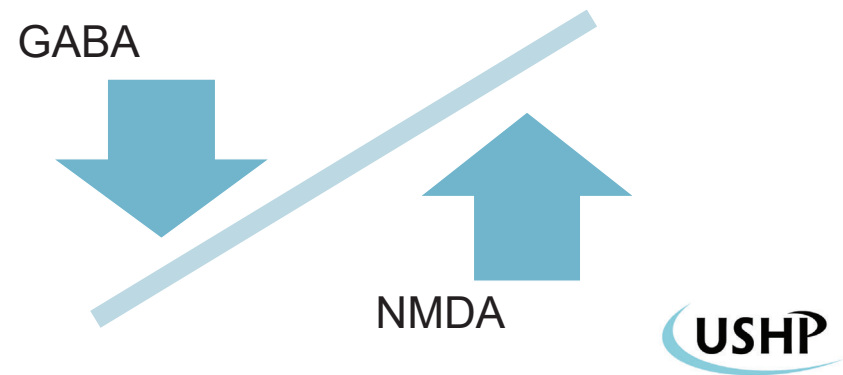
## Pathophysiology Continued



Davies M. The role of GABA<sub>A</sub> receptors in mediating the effects of alcohol in the central nervous system. *J Psychiatry Neurosci*. 2003;28(4):263-274.

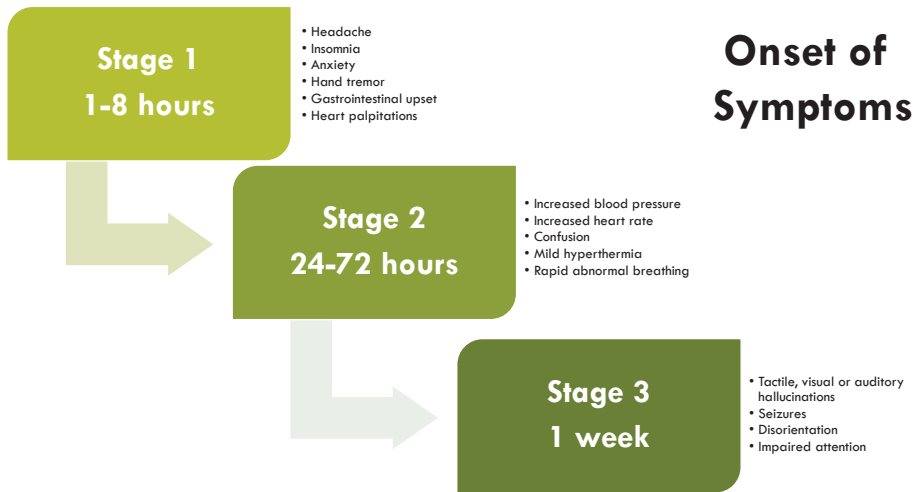
11

## Pathophysiology Continued



Davies M. The role of GABA<sub>A</sub> receptors in mediating the effects of alcohol in the central nervous system. *J Psychiatry Neurosci*. 2003;28(4):263-274.

12



Kelley R, January 7 NIJ, 2022. Alcohol Withdrawal Symptoms, Timeline & Detox Process. American Addiction Centers. Accessed February 13, 2022.

13

## Risk Factors



Early alcohol use

Family history

Genetics

Parental factors



Management of moderate and severe alcohol withdrawal syndromes - UpToDate.

14

## Patient Case

AA is a 35-year-old male with a history of alcohol withdrawal (started when 13 yo) who presents to ED for alcohol intoxication, headache and nausea. He is extremely agitated and states that he drank about 1/5 of vodka and a 6 pack of beer sometime in the last 24 hours. He was admitted to the hospital earlier this year for AWS complicated by a severe metabolic acidosis and seizure. Denies any other substance abuse. He denies visual/auditory hallucinations.

BP: 157/103

HR: 132

RR: 25

Temperature: 37 C

ETOH: 302 mg/dL

ABW 100 kg

IBW 73 kg



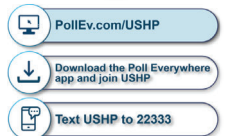
15

## Audience Response Question

Respond at [PollEv.com/ushp](https://poll-ev.com/ushp)  
Text USHP to 22333 once to join, then A, B, or C

**What stage of withdrawal is AA in based on is presenting symptoms?**

- |         |          |
|---------|----------|
| Stage 1 | <b>A</b> |
| Stage 2 | <b>B</b> |
| Stage 3 | <b>C</b> |



16

# Assessment Tools

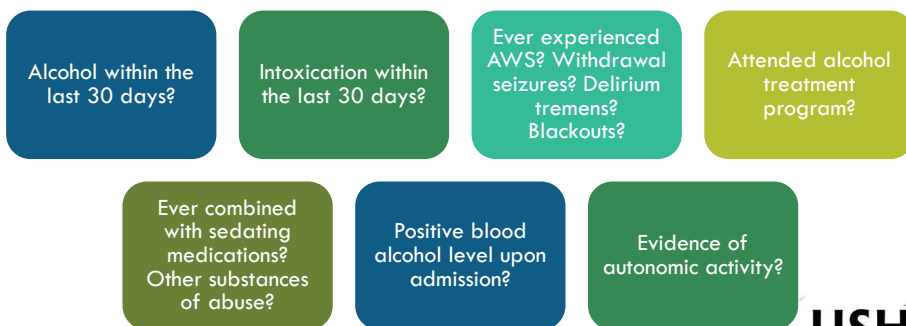


## Prediction of Alcohol Withdrawal Severity Scale (PAWSS)



- Tool to identify patients at risk for developing complicated alcohol withdrawal

## PAWSS Scoring Calculation



## PAWSS Scoring Calculation

### Average Risk Score:

- Answered yes on 0-3 questions

### High Risk Score:

- Answered yes on 4-10 questions



## Patient Case

AA is a 35-year-old male with a history of alcohol withdrawal (started when 13 yo) who presents to ED for alcohol intoxication, headache and nausea. He is extremely agitated and states that he drank about 1/5 of vodka and a 6 pack of beer sometime in the last 24 hours. He was admitted to the hospital earlier this year for AWS complicated by a severe metabolic acidosis and seizure. Denies any other substance abuse. He denies visual/auditory hallucinations.

BP: 157/103

HR: 132

RR: 25

Temperature: 37 C

ETOH: 302 mg/dL

ABW 100 kg

IBW 73 kg



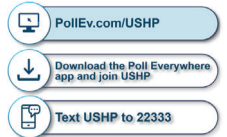
21

## Audience Response Question

Respond at [PollEv.com/ushp](https://PollEv.com/ushp)  
Text USHP to 22333 once to join, then A, B, or C

What is AA's PAWSS score?

3	A
5	B
10	C



22

## Other Assessment Tools



23



## Clinical Institute Withdrawal Assessment for Alcohol (CIWA-Ar)

- Originally published 1981
- Developed to assess the severity of alcohol withdrawal
- Aimed at evaluating all patients suspected of being at risk to have alcohol withdrawal

CIWA-Ar for Alcohol Withdrawal - MDCalc

24

**Nausea? Tremor? Paroxysmal sweats? Anxiety?  
Agitation? Headache? Tactile disturbances? Auditory?  
Visual?**

- Not Present - Extremely Severe (0-7)

**Oriented?**

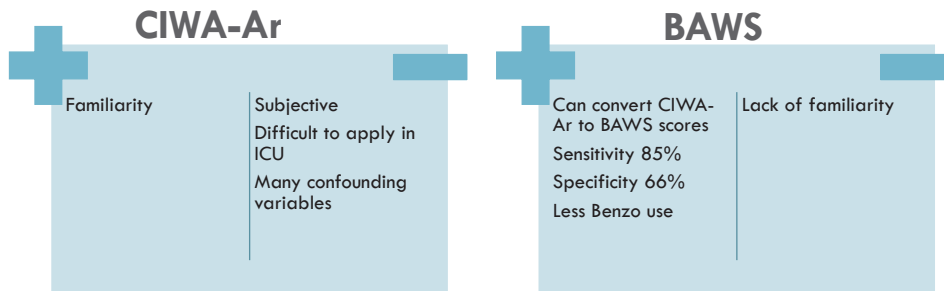
- Oriented - Disoriented (0-4)

## CIWA-Ar Scoring Calculation

## Brief Alcohol Withdrawal Scale (BAWS)

Symptom	0	1	2	3
Tremor	None	Felt, not visible	With arms extended	At rest
Diaphoresis	None	Visible	Beads of sweat	Drenched
Agitation	Calm	Anxious	Agitated	Violent
Confusion	Oriented	Disoriented to time	Disoriented to time and place	Disoriented
Hallucinations	None	Vague	More defined	Severe

## Which one is best?



## Treatment

## Treatment

Phenobarbital

vs

Benzodiazepines



Management of moderate and severe alcohol withdrawal syndromes - UpToDate.

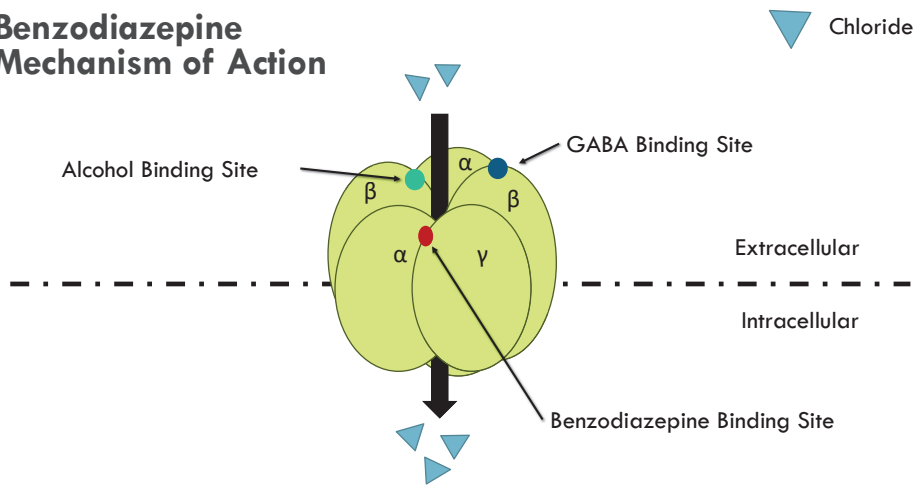
29

Benzodiazepines



30

## Benzodiazepine Mechanism of Action



Lorazepam - Lexicomp.

31

## Benzodiazepine Dosing

Benzodiazepine	Route	Dose	Onset	Half-life
Chlordiazepoxide	PO	<ul style="list-style-type: none"> <li>25-100 mg PRN</li> <li>50 mg every 6 hours for 1 day, then 25 mg every 6 hours for 2 days</li> </ul>	30 minutes - 2 hours	24-48 hours
Diazepam	IV PO	<ul style="list-style-type: none"> <li>5-20 mg PRN</li> <li>10 mg every 6 hours for 1 day, then 5 mg every 6 hours for 2 days</li> </ul>	IV: 10 minutes PO: 1 hours	33-48 hours
Lorazepam	IV PO	<ul style="list-style-type: none"> <li>2-4 mg PRN</li> <li>6-8 mg/day then 4-day taper</li> </ul>	IV: 10 minutes PO: 2 hours	12-14 hours

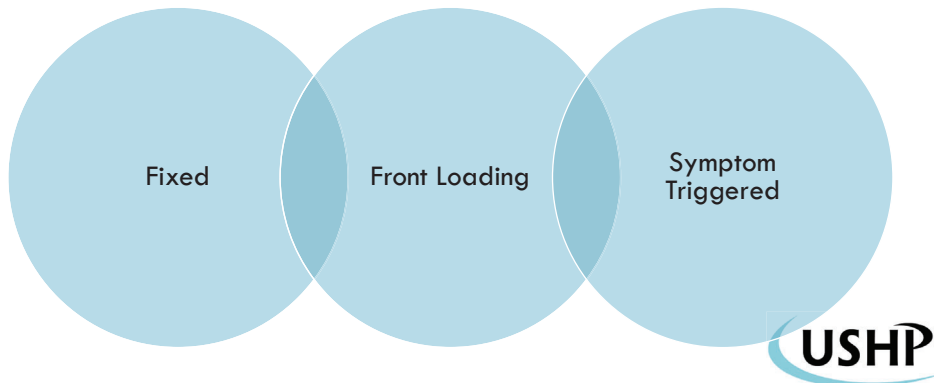


Chlordiazepoxide, Diazepam, Lorazepam - Lexicomp.

32



## Benzodiazepine Dosing Strategies



Management of moderate and severe alcohol withdrawal syndromes - UpToDate.

33

## Dosing Considerations

- Pregnancy
  - Short acting benzodiazepine
  - Dose reduced benzodiazepine preferred
- Renal
  - Short acting benzodiazepine
- Hepatic
  - Short acting benzodiazepine
  - Dose reduced benzodiazepine preferred



Clonazepam, Diazepam, Lorazepam - Lexicomp.

34

## Monitoring

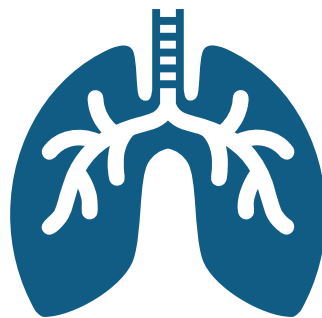
Respiratory depression

Hypotension

Paradoxical reactions

Anteretrograde amnesia

Nausea/vomiting



Clonazepam, Diazepam, Lorazepam - Lexicomp.

35

## Benefits

- Clinical standard of care
- Improves discomfort associated with acute withdrawal
- Decreases risk of progression to:
  - Seizures
  - Delirium

Management of moderate and severe alcohol withdrawal syndromes - UpToDate.

36

## Challenges

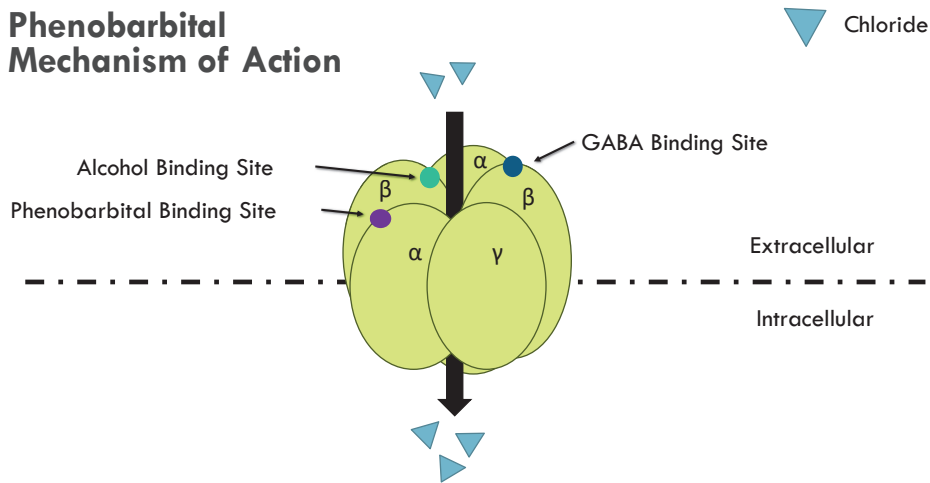
- Patients with chronic heavy alcohol use can develop cross-tolerance
- Increased risk of rebound withdrawal symptoms
- Increased risk of post-treatment drinking
- Other Risks:
  - Respiratory depression
  - Encephalopathy
  - Agitation in medically hospitalized patients



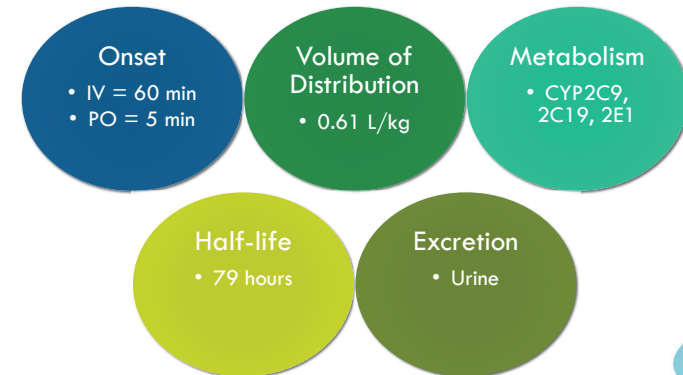
## Phenobarbital

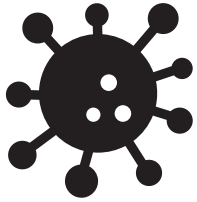


## Phenobarbital Mechanism of Action



## Phenobarbital Pharmacokinetics





## Phenobarbital Interactions \*\*

Aripiprazole

Quetiapine

Risperidone

Ticagrelor

Nifedipine

Azole Antifungals

Antiretrovirals

\*\*not all inclusive

## Storage of Compounded Dose

### Oral

- Store between 20°C and 25°C (68°F and 77°F)
- Protect from light

### Injection

- Store between 20°C and 25°C (68°F and 77°F)



USHP

## Monitoring

- Respiratory depression
- Hypotension
- Drowsiness
- Nausea/vomiting
- Risk of necrosis if extravasation occurs
- Rash

## Contraindications for Use

- Hypersensitivity reactions to phenobarbital
- Marked hepatic impairment:
  - Caution in patients with hepatic impairment
  - Avoid use in patients with hepatic encephalopathy
- Dyspnea or airway obstruction
- Porphyria
- Pregnancy



USHP

## Benefits and Challenges

- Benefits:
  - Long half life
  - Not a narrow therapeutic index drug
  - Levels are available
- Challenges:
  - Risk of respiratory depression
  - Not the clinical standard of care

Indication	Phenobarbital Level	Toxicity Severity
Seizures	10-40	N/A
Toxicity	> 50	Mild
Alcohol Withdrawal	> 65	Severe



## Audience Response Question

Respond at [PollEv.com/ushp](https://PollEv.com/ushp)  
Text USHP to 22333 once to join, then A or B

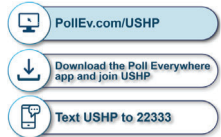
Based on patient characteristics, what agents are you most comfortable using for AA?

Benzodiazepines

A

Phenobarbital

B



## Patient Case

Your ED physician is interested in starting phenobarbital for AA. After her interview, she hands you a list of his current medications

Folic acid 1 mg once daily  
Thiamine 100 mg once daily  
Quetiapine 100 mg once nightly  
Bupropion 100 mg once daily



## Audience Response Question

Respond at [PollEv.com/ushp](https://PollEv.com/ushp)  
Text USHP to 22333 once to join, then A, B, C, or D

What medications on AA's home list are you concerned about?

bupropion

A

quetiapine

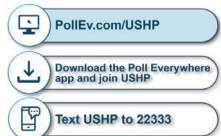
B

folic acid

C

thiamine

D



# Evidence

## Summary of Evidence

ED

Acute  
Care

ICU



49



50

# Safety and Efficacy in the ED

**Benzodiazepines vs  
barbiturates for alcohol  
withdrawal:  
Analysis of 3 different  
treatment protocols**  
Nelson et al. 2019

### Study Design

- Retrospective observational cohort study

### Population

- ED patients

### Intervention

- Phenobarbital protocol
- Lorazepam + phenobarbital protocol

### Comparator

- Diazepam protocol

### Outcome

- No difference in:
  - Rate of mechanical ventilation
  - Rate of ICU admission from the ED

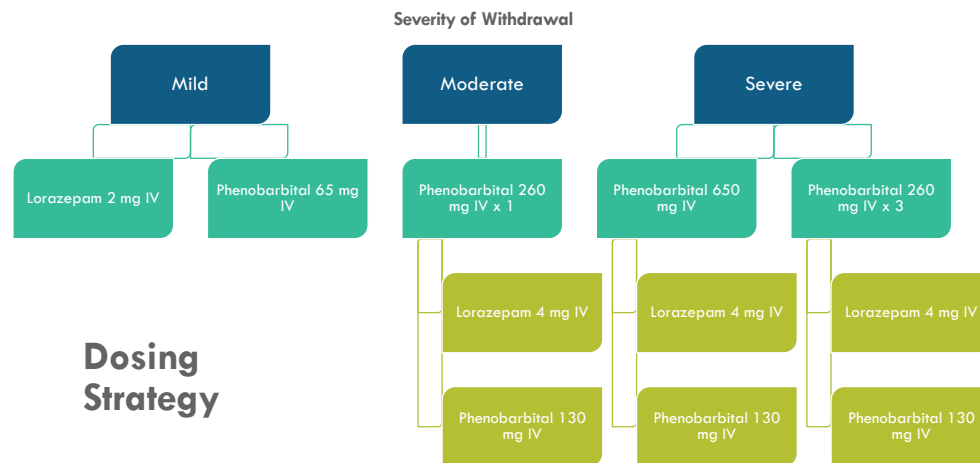


51



52

Nelson AC et al. Benzodiazepines vs barbiturates for alcohol withdrawal: Analysis of 3 different treatment protocols. Am J Emerg Med. 2019;37(4):733-736.



Nelson AC. Benzodiazepines vs barbiturates for alcohol withdrawal: Analysis of 3 different treatment protocols. Am J Emerg Med. 2019;37(4):733-736.

53

## Phenobarbital For Acute Alcohol Withdrawal: A Prospective Randomized Double-blind Placebo-controlled Study

Rosenson et al. 2013

### Study Design

- Prospective, randomized, double-blind, placebo-controlled study

### Population

- ED patients

### Intervention

- Phenobarbital protocol + symptom triggered lorazepam
- Phenobarbital 10 mg/kg IV

### Comparator

- Placebo

### Outcome

- Fewer ICU admissions
- No difference in:
- Adverse events



Rosenson et al. Phenobarbital for acute alcohol withdrawal: a prospective randomized double-blind placebo-controlled study. J Emerg Med. 2013;44(3):592-598.e2.

54

## Summary of Evidence



Study	Nelson et al. 2019	Rosenson et al. 2013
<b>Dosing Strategy</b>	Alcohol withdrawal severity based	10 mg/kg IV x 1 + symptom triggered lorazepam
<b>Outcome</b>	No difference in: <ul style="list-style-type: none"> <li>• Rate of mechanical ventilation</li> <li>• ICU admission from the ED</li> </ul>	<ul style="list-style-type: none"> <li>• Decreased ICU admissions</li> <li>• No difference in adverse events</li> </ul>
<b>Is phenobarbital safe and effective?</b>	Yes	Yes

## Safety and Efficacy in Acute Care



55

56

## Use of Phenobarbital in Alcohol Withdrawal Management: A Retrospective Comparison Study of Phenobarbital and Benzodiazepines for Acute Alcohol Withdrawal Management in General Medical Patients

Nisavic et al. 2019

### Study Design

- Retrospective cohort study

### Population

- General medicine patients

### Intervention

- Phenobarbital protocol

### Comparator

- Fixed dose benzodiazepine protocol

### Outcome

- Similar outcomes:
  - Development of AWS-related complications
  - Hospital length of stay
  - ICU admission rates/length of stay
  - Adverse events
  - Discharge against medical advice



Nisavic M et al. Use of Phenobarbital in Alcohol Withdrawal Management - A Retrospective Comparison Study of Phenobarbital and Benzodiazepines for Acute Alcohol Withdrawal Management in General Medical Patients. *Psychosomatics*. 2019;60(5):458-467.

57

## Phenobarbital for Acute Alcohol Withdrawal Management in Surgical Trauma Patients—A Retrospective Comparison Study

Nejad et al. 2020

### Study Design

- Retrospective cohort study

### Population

- Surgical Trauma Patients on all floors (ED to ICU)

### Intervention

- Phenobarbital protocol

### Comparator

- Fixed dose benzodiazepine protocol

### Outcome

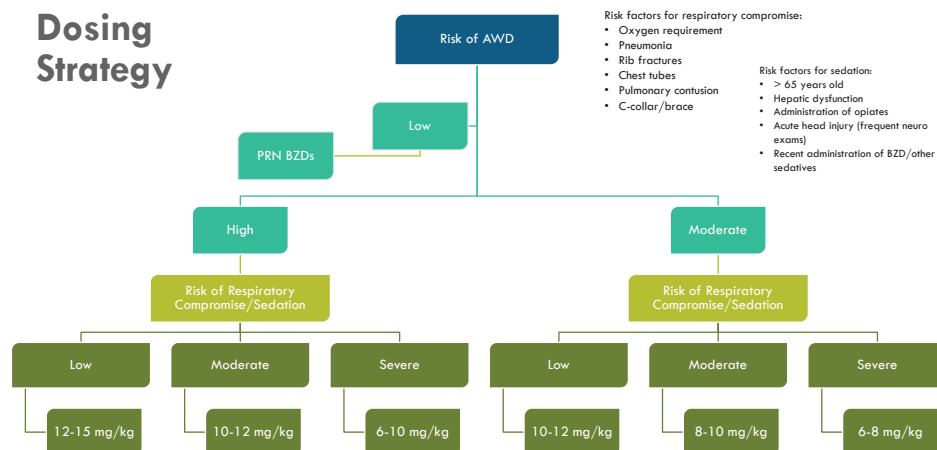
- Less alcohol withdrawal delirium
- Less alcohol withdrawal syndrome
- Less adverse side effects



Nejad S et al. Phenobarbital for Acute Alcohol Withdrawal Management in Surgical Trauma Patients: A Retrospective Comparison Study. *Psychosomatics*. 2020;61(4):327-335.

58

## Dosing Strategy



Nisavic M et al. Use of Phenobarbital in Alcohol Withdrawal Management - A Retrospective Comparison Study of Phenobarbital and Benzodiazepines for Acute Alcohol Withdrawal Management in General Medical Patients. *Psychosomatics*. 2019;60(5):458-467.

59

## Summary of Evidence

### Acute Care

Study	Nejad et al. 2020	Nisavic et al. 2019
<b>Dosing Strategy</b>	Risk of AWD based	
<b>Outcome</b>	Less: <ul style="list-style-type: none"> <li>• Delirium</li> <li>• Adverse events</li> </ul>	No difference in: <ul style="list-style-type: none"> <li>• Development of complications</li> <li>• Hospital length of stay</li> <li>• ICU admission rates</li> <li>• ICU length of stay</li> <li>• Adverse events</li> <li>• Discharge against medical advice</li> </ul>
<b>Is phenobarbital safe and effective?</b>	Yes	Yes

Nejad S et al. Phenobarbital for Acute Alcohol Withdrawal Management in Surgical Trauma Patients: A Retrospective Comparison Study. *Psychosomatics*. 2020;61(4):327-335.

60

# Safety and Efficacy in the ICU



61

## Treatment of Alcohol Withdrawal Syndrome: Phenobarbital vs CIWA-Ar Protocol

Tidwell et al. 2018

### Study Design

- Retrospective cohort study

### Population

- Medical ICU patients

### Intervention

- Phenobarbital protocol

### Comparator

- Symptom triggered benzodiazepine protocol

### Outcome

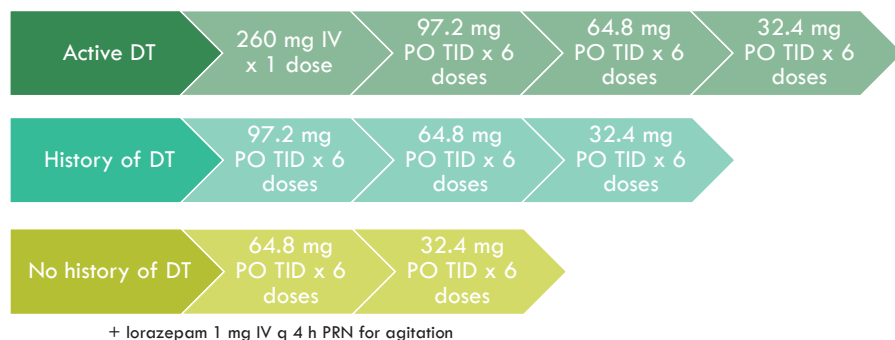
- Shorter ICU stay
- Shorter hospital stay
- Less mechanical ventilation
- Less use of adjunctive agents



62

Tidwell WP, Thomas TL, Poullot JD, Conosca AE, Webber AJ. Treatment of Alcohol Withdrawal Syndrome: Phenobarbital vs CIWA-Ar Protocol. Am J Crit Care. 2018;27(6):454-460.

## Dosing Strategy



## Phenobarbital and symptom-triggered lorazepam versus lorazepam alone for severe alcohol withdrawal in the intensive care unit

Nguyen et al. 2020

### Study Design

- Retrospective cohort study

### Population

- ICU Patients

### Intervention

- Phenobarbital protocol

### Comparator

- Symptom triggered benzodiazepine protocol

### Outcome

- Duration of treatment shorter
- Similar ICU length of stay
- Lower CIWA-Ar from baseline at 24 hours
- Similar in adverse events



64

Nguyen TA, Lam SW. Phenobarbital and symptom-triggered lorazepam versus lorazepam alone for severe alcohol withdrawal in the intensive care unit. Alcohol. 2020;82:23-27.

Tidwell WP, Thomas TL, Poullot JD, Conosca AE, Webber AJ. Treatment of Alcohol Withdrawal Syndrome: Phenobarbital vs CIWA-Ar Protocol. Am J Crit Care. 2018;27(6):454-460.

63



## Summary of Evidence

### ICU

Study	Tidwell et al. 2018	Nguyen et al. 2020
Dosing Strategy	Risk/presence of DT based	Unspecified
Outcome	<ul style="list-style-type: none"> <li>• Shorter ICU stay</li> <li>• Shorter hospital stay</li> <li>• Less mechanical ventilation</li> <li>• Less use of adjunctive agents</li> </ul>	<ul style="list-style-type: none"> <li>• Shorter treatment duration</li> <li>• Lower CIWA-Ar from baseline at 24 hours</li> <li>• Similar in:                             <ul style="list-style-type: none"> <li>• Adverse events</li> <li>• ICU length of stay</li> </ul> </li> </ul>
Is phenobarbital safe and effective?	Yes	Yes

## Dosing Strategies



65

65

66

## Considerations

- Was initial dose of phenobarbital enough?
- Does my patient need additional titration?
- Which weight should I use to base dosing recommendations?
- What's the cumulative dose this patient has received throughout their stay?

## Dosing Pearls

Load based on patient's IBW

Titrate as needed

Do not exceed cumulative dose of 20 mg/kg IBW

- Consider other sedating medications patient has received
- This may require a smaller cumulative dose (5-10 mg/kg)

Give total cumulative dose within 48 hours

- Significant metabolism may occur if administered over a longer time

Use caution in severe obesity (BMI >40)

Obtain a phenobarbital level



67

Pantwi R, et al. Update on Phenobarbital for Alcohol Withdrawal Syndrome in Intensive Care. Journal of Clinical Intensive Care and Medicine. 2019;4(1):036-039.

68

## Patient Case

AA is a 35-year-old male with a history of alcohol withdrawal (started when 13 yo) who presents to ED for alcohol intoxication, headache and nausea. He is extremely agitated and states that he drank about 1/5 of vodka and a 6 pack of beer sometime in the last 24 hours. He was admitted to the hospital earlier this year for AWS complicated by a severe metabolic acidosis and seizure. Denies any other substance abuse. He denies visual/auditory hallucinations.

BP: 157/103

HR: 132

RR: 25

Temperature: 37 C

ETOH: 302 mg/dL

ABW 100 kg

IBW 73 kg



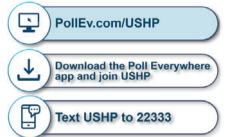
69

## Audience Response Question

Respond at [PollEv.com/ushp](https://PollEv.com/ushp)  
Text USHP to 22333 once to join, then A, B, C, or D

What is an appropriate phenobarbital dosing strategy for AA?

- |   |          |
|---|----------|
| Load only: 10 - 15 mg/kg IV over 2 days   | <b>A</b> |
| Titration: 10 mg/kg IV x 1, 65 mg PO x 6 doses, 32 mg PO x 6 doses                  | <b>B</b> |
| Titration: 10 mg/kg IV x 1, then 260 mg IV x 1 dose for moderate to severe symptoms | <b>C</b> |
| Titration: 10 mg/kg IV x 1, then 130 mg IV x 1 dose for mild symptoms               | <b>D</b> |



70

## What's Next?



71

(PARTI) Phenobarbital vs Ativan for Alcohol Withdrawal in the Intensive Care Unit

- Prospective, open-label, randomized, controlled trial
- March 2022
- NCT04156464

(PHENOMANAL) Phenobarbital for Severe Acute Alcohol Withdrawal Syndrome

- Prospective, placebo controlled, randomized
- November 2022
- NCT03586089

Ativan & Phenobarbital Versus Ativan for Refractory Alcohol Withdrawal Treatment in the Intensive Care Unit, [clinicaltrials.gov](https://clinicaltrials.gov), 2020.  
Unity Health Toronto, PHENOMANAL for the Management of Severe Acute Alcohol Withdrawal Syndrome (PHENOMANAL) A Prospective Randomized Feasibility Study, [clinicaltrials.gov](https://clinicaltrials.gov), 2020.

72

## References

- \* Aulakh B. Phenobarbital Versus Ativan for Refractory Alcohol Withdrawal Treatment in the Intensive Care Unit. *clinicaltrials.gov*; 2020. Accessed February 10, 2022. <https://clinicaltrials.gov/ct2/show/NCT04156464>
- \* Prediction of Alcohol Withdrawal Severity Scale - MDCalc. Accessed February 13, 2022. <https://www.mdcalc.com/prediction-alcohol-withdrawal-severity-scale>
- \* Phenobarbital - Lexicomp. Accessed February 13, 2022. <http://online.lexi.com.ezproxy.lib.utah.edu/lco/action/homejsessionid=e02a04aafb82e5a7cf5a563f04d5?siteid=4>
- \* Management of moderate and severe alcohol withdrawal syndromes - UpToDate. Accessed February 13, 2022. <https://www.uptodate.com/contents/search>
- \* Lorazepam - Lexicomp. Accessed February 13, 2022. <http://online.lexi.com.ezproxy.lib.utah.edu/lco/action/homejsessionid=e02a04aafb82e5a7cf5a563f04d5?siteid=4>
- \* Diazepam - Lexicomp. Accessed February 13, 2022. <http://online.lexi.com.ezproxy.lib.utah.edu/lco/action/homejsessionid=e02a04aafb82e5a7cf5a563f04d5?siteid=4>
- \* CIWA-Ar for Alcohol Withdrawal - MDCalc. Accessed February 13, 2022. <https://www.mdcalc.com/ciwa-ar-alcohol-withdrawal>
- \* Chlordiazepoxide - Lexicomp. Accessed February 13, 2022. <http://online.lexi.com.ezproxy.lib.utah.edu/lco/action/homejsessionid=e02a04aafb82e5a7cf5a563f04d5?siteid=4>
- \* Alcohol Use Disorder: What It Is, Risks & Treatment. Cleveland Clinic. Accessed February 13, 2022. <https://my.clevelandclinic.org/health/diseases/3909-alcoholism>
- \* Davies M. The role of GABAA receptors in mediating the effects of alcohol in the central nervous system. *J Psychiatry Neurosci*. 2003;28(4):263-274.
- \* Kelley R, January 7 NLU, 2022. Alcohol Withdrawal: Symptoms, Timeline & Detox Process. American Addiction Centers. Accessed February 13, 2022. <https://americanaddictioncenters.org/withdrawal-timeline-treatments/alcohol>
- \* Nejad S, Nisavic M, Larentzakis A, et al. Phenobarbital for Acute Alcohol Withdrawal Management in Surgical Trauma Patients-A Retrospective Comparison Study. *Psychosomatics*. 2020;61(4):327-335. doi:10.1016/j.psypm.2020.01.008
- \* Nelson AC, Kehoe J, Sankoff J, Mintzer D, Taub J, Kaucher KA. Benzodiazepines vs barbiturates for alcohol withdrawal: Analysis of 3 different treatment protocols. *Am J Emerg Med*. 2019;37(4):733-736. doi:10.1016/j.ajem.2019.01.002



## References

- \* Nguyen TA, Lam SW. Phenobarbital and symptom-triggered lorazepam versus lorazepam alone for severe alcohol withdrawal in the intensive care unit. *Alcohol*. 2020;82:23-27. doi:10.1016/j.alcohol.2019.07.004
- \* Nisavic M, Nejad SH, Isenberg BM, et al. Use of Phenobarbital in Alcohol Withdrawal Management - A Retrospective Comparison Study of Phenobarbital and Benzodiazepines for Acute Alcohol Withdrawal Management in General Medical Patients. *Psychosomatics*. 2019;60(5):458-467. doi:10.1016/j.psypm.2019.02.002
- \* Rostegar DA, Applewhite D, Alvanzo AAH, Welsh C, Niessen T, Chen ES. Development and implementation of an alcohol withdrawal protocol using a 5-item scale, the Brief Alcohol Withdrawal Scale (BAWS). *Subst Abuse*. 2017;38(4):394-400. doi:10.1080/08897077.2017.1354119
- \* Rosenson J, Clements C, Simon B, et al. Phenobarbital for acute alcohol withdrawal: a prospective randomized double-blind placebo-controlled study. *J Emerg Med*. 2013;44(3):592-598.e2. doi:10.1016/j.jemermed.2012.07.056
- \* Saltz R. Introduction to Alcohol Withdrawal. *Alcohol Health Res World*. 1998;22(1):5-12.
- \* Tidwell WP, Thomas TL, Pouliot JD, Canonico AE, Webber AJ. Treatment of Alcohol Withdrawal Syndrome: Phenobarbital vs CIWA-Ar Protocol. *Am J Crit Care*. 2018;27(6):454-460. doi:10.4037/ajcc.2018.745
- \* Unity Health Toronto. PHENObarbital for the MANagement of Severe Acute Alcohol Withdrawal Syndrome (PHENOMANAL): A Prospective Randomized Feasibility Study. *clinicaltrials.gov*; 2020. Accessed February 10, 2022. <https://clinicaltrials.gov/ct2/show/NCT03586089>
- \* Alcohol Facts and Statistics | National Institute on Alcohol Abuse and Alcoholism (NIAAA). Accessed February 13, 2022. <https://www.niaaa.nih.gov/publications/brochures-and-fact-sheets/alcohol-facts-and-statistics>
- \* Banerjee N. Neurotransmitters in alcoholism: A review of neurobiological and genetic studies. *Indian J Hum Genet*. 2014;20(1):20-31. doi:10.4103/0971-6866.132750
- \* Parthvi R, Agne P. Update on Phenobarbital for Alcohol Withdrawal Syndrome in Intensive Care. *Journal of Clinical Intensive Care and Medicine*. 2019;4(1):036-039. doi:10.29328/journal.icim.1001023
- \* A Comparison Of Baws (brief Alcohol Withdrawal Scale) With Ciwa-ar To Diagnose The Severity Of Alcohol Withdrawal In Hospitalized Medical Patients. Accessed February 14, 2022. <https://shmastracts.org/abstract/a-comparison-of-baws-brief-alcohol-withdrawal-scale-with-ciwa-ar-to-diagnose-the-severity-of-alcohol-withdrawal-in-hospitalized-medical-patients/>

