TEMPLE UNIVERSITY HOSPITAL, INC.
ADMINISTRATIVE GUIDELINE

Number: TUH INC-ADMIN-MM-GUIDELINES-3
Title: GUIDELINE: PHENOBARBITAL FOR SEDATIVE/HYPNOTIC WITHDRAWAL
Effective Date: 09/26/2024
Last Revised: 2/07/2025
Last Reviewed: NEW
Attachments: **Attachment A:** Prediction of Alcohol Withdrawal Severity Scale (PAWSS)
References:

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2. 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/ajcc2018745
3. Hammond DA, Rowe JM, Wong A, Wiley TL, Lee KC, Kane-Gill SL. Patient Outcomes Associated With Phenobarbital Use With or Without Benzodiazepines for Alcohol Withdrawal Syndrome: A Systematic Review. Hosp Pharm. 2017;52(9):607-616. doi:10.1177/0018578717720310
4. Mo Y, Thomas MC, Karras GE Jr. Barbiturates for the treatment of alcohol withdrawal syndrome: A systematic review of clinical trials. J Crit Care. 2016;32:101-107. doi:10.1016/j.jcrc.2015.11.022
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6. Nisavic M, Nejad SH, Isenberg BM, Bajwa EK, Currier P, Wallace PM, Velmahos G, Wilens T. 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 Sep-Oct;60(5):458-467. doi: 10.1016/j.psym.2019.02.002.
7. Maldonado JR, Sher Y, Das S, Hills-Evans K, Frenklach A, Lolak S, Talley R, Neri E. Prospective Validation Study of the Prediction of Alcohol Withdrawal Severity Scale (PAWSS) in Medically Ill Inpatients: A New Scale for the Prediction of Complicated Alcohol Withdrawal Syndrome. Alcohol Alcohol. 2015 Sep;50(5):509-18. doi: 10.1093/alcalc/agv043.

SCOPE

This guideline shall apply to Temple University Hospital, Inc. (TUH), including TUH-Main Campus (TUH-MC), TUH-Episcopal Campus (TUH-EC), and TUH Jeanes Campus (TUH-JC).

PURPOSE

The purpose of this guideline is to provide general dosing and monitoring recommendations for the use of phenobarbital in the treatment or prevention of sedative and/or hypnotic withdrawal. This includes treatment or prevention of withdrawal due to alcohol, benzodiazepines, or related substances. These guidelines are intended to apply to use of phenobarbital in both critical care areas (intensive care units, emergency department) as well as general medicine and/or surgical patient care floors.

DEFINITIONS

CIWA – Clinical Institute Withdrawal Assessment
DOAC – Direct Oral Acting Anticoagulant
HIV – Human Immunodeficiency Virus
IBW – Ideal Body Weight
IM - Intramuscular
IV – Intravenous
MINDS – Minnesota Detoxification Scale
RASS – Richmond Agitation Sedation Scale
PAWSS – Prediction of Alcohol Withdrawal Severity Scale

GUIDELINE

1. **Addiction Medicine Consult**
   a. Consider addiction medicine consult as needed for assistance in dosing/appropriate patient selection
2. **Indications for Use and Appropriate Patient Selection**
   a. Treatment of active alcohol/sedative/hypnotic withdrawal and/or prevention of withdrawal syndrome in patients who are at high risk for its development (e.g. PAWSS score ≥ 4)
      a. Refer to ATTATCHMENT A for calculation of Prediction of Alcohol Withdrawal Severity Scale (PAWSS)
         i. 0 – 3: Average Risk for development of complicated withdrawal
         ii. ≥ 4: High Risk for development of complicated withdrawal

   b. Transitioning from benzodiazepines to phenobarbital may be warranted to advance care. However, the concomitant use of phenobarbital and benzodiazepines may result in additive adverse effects. Caution is advised if utilizing continued concomitant therapy.

Use with Caution	Avoid Use
Unclear history of alcohol/sedative/hypnotic use dependence	Concomitant severe liver disease, cirrhosis, and/or hepatic encephalopathy
Concomitant benzodiazepine use	Severe allergy to phenobarbital
History of multi-substance dependence	Significant drug-drug interaction (e.g. DOAC, HIV medications, antifungals, etc.)
If patient is already on phenobarbital for another chronic indication (e.g. seizure)	History of acute intermittent porphyria
Risk of respiratory compromise	Carotid Stenosis or acute CVA
Hemodynamic instability	Pregnancy

2. Concomitant Use with Benzodiazepines

a. The use of phenobarbital and benzodiazepines in combination may result in additive adverse effects. Caution is advised if utilizing continued concomitant therapy.

b. Consider the following when utilizing phenobarbital in addition to the benzodiazepine driven withdrawal protocols (i.e. CIWA, MINDS)

   i. If significant withdrawal persists at any time after initial loading dose, adjunctive (one-time) phenobarbital doses (e.g. 65- 260 mg IV once) are recommended per dosing below, rather than symptom-triggered benzodiazepines.

   ii. Phenobarbital taper may be used as replacement for standing benzodiazepines within the above withdrawal protocols.

   iii. As needed (PRN) phenobarbital doses should **NOT** be utilized in conjunction with the benzodiazepine based withdrawal protocols.

3. Monitoring and Documentation of Phenobarbital Therapy

a. Vital signs (blood pressure, heart rate, respiratory rate) should be assessed 15 minutes after administration of IV loading/initial dose and 30-60 minutes after oral loading/initial dose; followed by at least every 2 to 4 hours for the first 24 hours of therapy.

b. Hold further phenobarbital doses and discuss with the provider if any of the following occur:
   i. Blood pressure < 90/60 mmHg
   ii. Heart rate < 50 bpm
   iii. Respiratory rate < 8 bpm
   iv. RASS score < (-1) [if applicable], over sedation, or significant change in mental status

c. Treatment should be tailored to clinical response.
   i. Improvement in agitation, tachycardia, hypertension, tremulousness, and diaphoresis may be used to indicate positive treatment response
   ii. If patients have received 15-20 mg/kg/day of phenobarbital with no clinical improvement, alternate diagnoses should be considered, as most patients are adequately treated for alcohol/sedative/hypnotic withdrawal at these doses.

d. Serum phenobarbital concentration should not be routinely monitored during therapy.

3. General Dosing Algorithms

Severe Withdrawal or High Risk of Severe Withdrawal

(consider in patients with 2 or more (not attributable to another acute disease state) of the following:

- **Severe withdrawal**

Heart rate > 120 bpm, diastolic blood pressure > 90 mmHg, temperature > 99 degrees Fahrenheit

Plus, experiencing either:

  - Two or more of the following: tremor, diaphoresis, restlessness
  - One of more of the following: agitation, altered mental status, seizure

- **High Risk of Severe Withdrawal**
  - PAWSS ≥ 4
- **Benzodiazepine resistant withdrawal**
  - Patients administered ≥ 40mg diazepam or ≥ 10mg lorazepam (or equivalent) in 1 hour with persistent or worsening withdrawal symptoms

<table>
<tr><th>Loading Dose</th><th colspan="2">Scheduled Dosing</th><th>Adjunctive Dosing</th></tr>
<tr><td rowspan="2">10 mg/kg (IBW) IV in 100 ml NS given over 30 min (RESTRICTED TO ICU/ED)

• Reevaluate 15-30 minutes after completion of loading dose

• If symptoms not improved within 30-60 minutes, see adjunctive dosing to treat ongoing symptoms

• Start scheduled maintenance dosing 6 to 24 hours after completion of loading dose</td><td>Days 1 –2</td><td>60 – 120 mg PO Q6 –Q12 hours
OR
65 – 130 mg IV/IM Q6 – Q12 hours

Tapering not always required but if tapering is required, patients should be ordered for IV/PO taper prior to transitions of care if appropriate for therapy to continue. Consider reducing TDD by 25-30% per day</td><td rowspan="2">65 – 260 mg IV/IM
OR
60 – 240 mg PO

May be ordered for breakthrough withdrawal in patients with continued signs and symptoms such as diaphoresis, tachycardia, restlessness, etc.

Provider must evaluate patient for adjunctive doses.

May repeat every 30-60 minutes to a max cumulative dose should not exceed 20 mg/kg/day</td></tr>
<tr><td>Days 3 – 5</td><td>30 – 60 mg PO Q12 hours
OR
32.5 – 65 mg IV/IM Q12 hours

Hold scheduled dose for over sedation or RASS < -1</td></tr>
<tr><td colspan="3">Administer IV Push doses (≤ 260) mg no faster than 5 minutes or 50 mg/min. IVPB doses (>260 mg) may be administered 50-100 mg/minute. Peak effect occurs approximately 15-30 minutes post IV dose and 5 hours post IM dose</td></tr>
</table>

Moderate Withdrawal

(patients not meeting above severe withdrawal symptoms or other indications)

<table>
<tr><th>Loading Dose</th><th colspan="2">Scheduled Dosing</th><th>Adjunctive Dosing</th></tr>
<tr><td rowspan="2">8 mg/kg (IBW) split dosing (IV or IM or PO)
40% initial
30% 3 hours later
30% 3 hours later

OR

5 mg/kg (IBW) IV in 100 ml NS given over 30 min

Reevaluate 15-30 minutes after completion of each dose

If symptoms not improved within 30-60 minutes, see adjunctive dosing to treat ongoing symptoms

Start scheduled maintenance dosing 6 to 24 hours after completion of loading dose</td><td>Days 1 –2</td><td>60 – 120 mg PO Q6 – Q12 hours
OR
65 – 130 mg IV/IM Q6 – Q12 hours

Tapering not always required but if tapering is required, patients should be ordered for IV/PO taper prior to transitions of care if appropriate for therapy to continue. Consider reducing TDD by 25-30% per day</td><td rowspan="2">65 – 260 mg IV/IM
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May be ordered for breakthrough withdrawal

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</table>

This document is designed to serve as a guideline and is not meant to be a strict procedure. Deviations from the treatment decisions established by this guideline or protocol are allowed, as deemed medically appropriate by the treating physicians, in order to optimize care for an individual patient.

APPROVALS

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Attachment A: Prediction of Alcohol Withdrawal Severity Scale (PAWSS)

Threshold Criteria (if yes to either, proceed with the rest of the criteria)		
Patient consumed any amount of alcohol within the last 30 days		If yes to either threshold criteria, proceed with scoring
Patient had a positive blood alcohol level upon admission		
Criteria	**Yes (1 point)**	**No (0 points)**
Have you been recently intoxicated or drunk within the last 30 days?		
Have you ever experienced previous episodes of alcohol withdrawal?		
Have you ever experienced withdrawal seizures?		
Have you ever experienced delirium tremens (DTs)?		
Have you ever undergone alcohol rehabilitation treatment (i.e., inpatient or outpatient treatment programs, or Alcoholics Anonymous attendance)?		
Have you ever experienced blackouts?		
Have you combined alcohol with other "downers" (e.g. benzodiazepines, barbiturates) during the last 90 days?		
Have you combined alcohol with any other substance of abuse during the last 90 days?		
Positive blood alcohol level (BAL) on presentation		
Evidence of increased autonomic activity (i.e., HR >120, tremor, sweating, agitation, nausea)?		
Total score		

Interpretation:
0-3: average risk of complicated AWS
≥4: high risk of complicated AWS

Complicated alcohol withdrawal syndrome (AWS) is defined as withdrawal hallucinosis, withdrawal-related seizures, or delirium tremens.