

Yale New Haven Health System Phenobarbital Guidance

The current guidance was developed within Yale-New Haven Health System to guide the treatment of alcohol withdrawal with phenobarbital.

These recommendations reflect YNHHS consensus based on review of existing evidence and guidelines. They do not replace clinical judgement.

This guidance is only current as of June 2024 and is routinely updated in response to feedback and new literature and guidelines.

Yale New Haven Health System Phenobarbital Guidance

Guidance for initiation of phenobarbital for alcohol withdrawal management

Determine which arm to start Phenobarbital (PHB) as monotherapy OR symptom triggered benzodiazepine

- [Patients who might benefit from PHB](#)
- [Contraindications](#) for phenobarbital
- [Alcohol Withdrawal Severity](#)
- [Risk factors](#) for severe alcohol withdrawal

Indications for phenobarbital (PHB)

- Hx of AWS and DTs
- Hx of AWS and success with PHB
- Trauma patients
- History of Resistant Alcohol Withdrawal (RAW) defined as severe withdrawal despite receiving high doses of benzodiazepines (>150 mg diazepam or >30 mg lorazepam in the first 3–4 hours of treatment)

Contraindications for phenobarbital

- Diagnosis of AWS is not entirely clear
- Decompensated liver cirrhosis
- [Child-Pugh Score](#) C
- Acute liver failure including acetaminophen overdose

Caution use of phenobarbital in hepatic dysfunction (AST/ALT >5x ULN) and in patients receiving medications metabolized via the cytochrome P450 enzymes

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Start phenobarbital monotherapy

Order phenobarbital order panel

- IV phenobarbital can be administered every 30-60 minutes (reaches peak level within 5 minutes)
- IM phenobarbital can be administered every 3 hours (reaches peak level within 5 hours)
- Patients may transfer to a non-ICU setting if they are stable 1 hour (IV) or 2 hours (IM) after the final loading dose
- [PHB IM versus IV recommendations](#)
- [Click here to open full phenobarbital guideline](#)

Check phenobarbital level 2 hours after IV loading dose or 5 hours after IM loading dose completion:

- **Order:** [phenobarbital level](#)
- [Recommendations on serum PHB levels](#)

PHB education



- IV route is recommended for acutely agitated patients or patients with complicated AWS requiring prompt management of AWS symptoms (withdrawal seizures)
- IM route is encouraged in non-acutely agitated patients to decrease the risk of adverse events (over-sedation and respiratory compromise)
 - Avoid intramuscular route in patients with platelet 50,000 per microliter, INR >2, or if the patient is therapeutically anticoagulated to decrease bleeding risk.
 - IM administration can be given in deltoid or gluteus muscles. Recommended maximum volumes for single IM injections are as follows. If the ordered volume exceeds the maximum recommended volume, split the ordered volume into multiple injections according to the following recommendations:
 - Well-developed typical adult = 3 mL
 - Thin or elderly adult = 2 mL

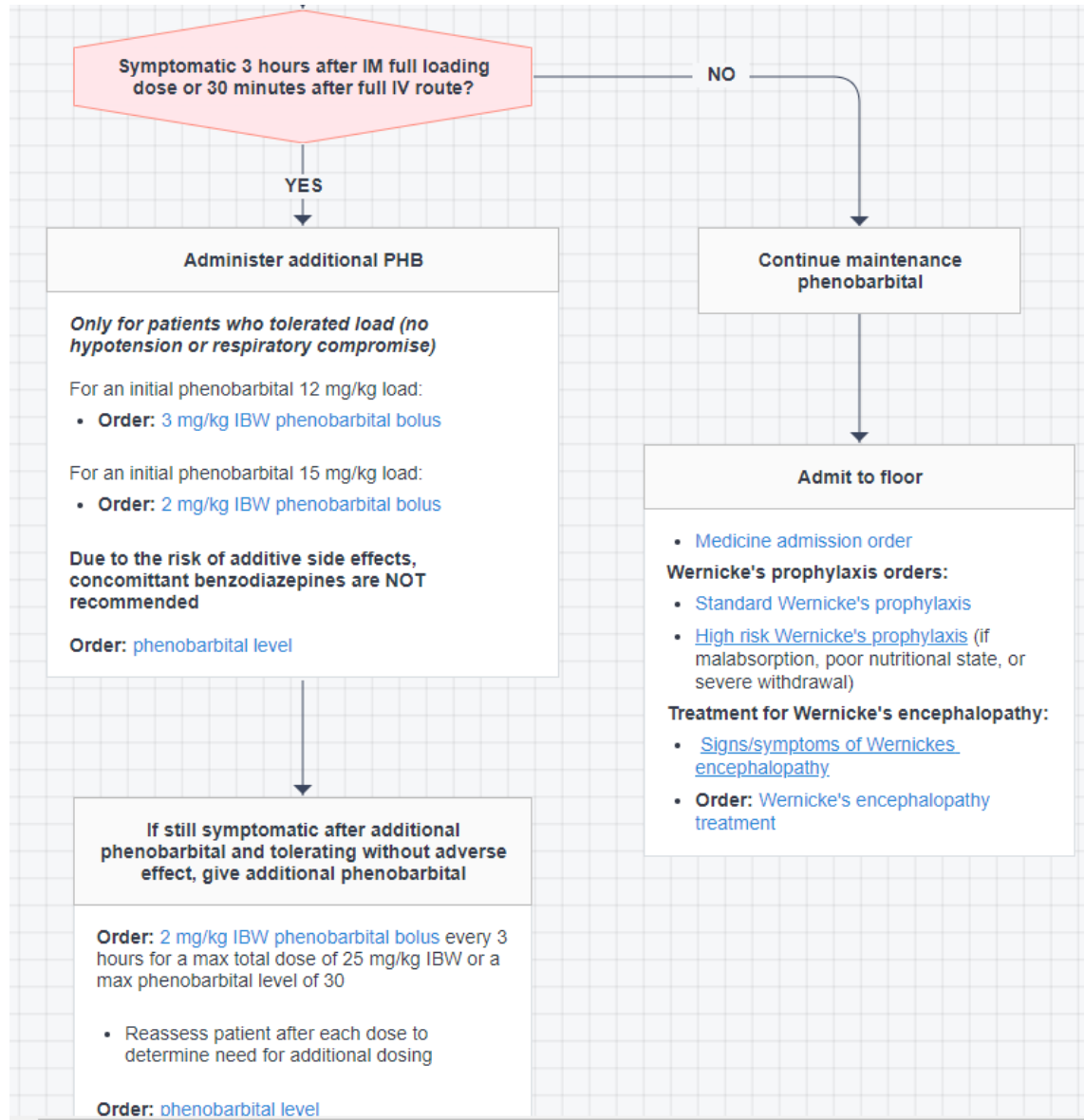
Recommendations on serum PHB levels



- There is NO target PHB level
- Serum levels > 30 mcg/ml have been associated with greater risk of adverse effects
- PHB 1mg/kg increases serum PHB level by 1.5 mcg/ml
- PHB level can be ordered [5 hours after IM](#) full loading dose or [2 hours if given via IV route](#)

Do NOT delay further PHB doses if the level has not resulted

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Phenobarbital order set:

▼ Phenobarbital Fixed-Dose Monotherapy

- [Phenobarbital Dosing Guideline for Management of Alcohol Withdrawal - Yale New Haven Health System](#)

▼ Phenobarbital

PHENobarbital (LUMINAL) Alcohol Withdrawal Medication Panel - Adults

If patient received greater than 20 mg lorazepam, 40 mg midazolam, or 100 mg diazepam in the last 12 hours then avoid PHENobarbital and consider alternative therapy.

Due to the risk of additive side effects concomitant benzodiazepines are NOT recommended for the management of alcohol withdrawal. Discontinue any standing or PRN benzodiazepine orders.

Benzodiazepine Administrations (last 12 hours)

None

- [Phenobarbital Dosing Guideline for Management of Alcohol Withdrawal - Yale New Haven Health System](#)

- Phenobarbital initial management (loading dose/maintenance regimen)
- Management of symptomatic patient who received phenobarbital loading dose (12 or 15 mg/kg)

Phenobarbital initial management (loading dose/maintenance regimen)

- Patient has NOT received any benzodiazepine in last 12 hours
- Patient received <20 mg lorazepam, 40 mg of midazolam, or 100 mg of diazepam in last 12 hours

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Patient has NOT received any benzodiazepine in last 12 hours

PHENobarbital (LUMINAL) level - may be timed to be drawn 5 hours after the end of loading dose on day 1 (\$\$\$)

1 PHENobarbital (LUMINAL) Loading Dose (Day 1)

Intramuscular route preferred, unless patient is acutely agitated, platelet <50,000 per microliter, INR >2 or therapeutically anticoagulated.

PHENobarbital (LUMINAL) IM Injection : 15 mg/kg total loading dose

PHENobarbital (LUMINAL) IV Push/IVPB : 15 mg/kg total loading dose

1 Taper/Maintenance Dosing (Day 2-5)

PHENobarbital (LUMINAL) tablet : Day 2 - 5

PHENobarbital (LUMINAL) IM : Day 2 - 5

PHENobarbital (LUMINAL) IV Push/IVPB : Day 2 - 5

1 CIWA-A or MINDS ASSESSMENT

CIWA-A for phenobarbital monotherapy (regular nursing floor)

Routine, CONTINUOUS, This is the CIWA protocol for patients on phenobarbital monotherapy on the floor. It is intended to identify alcohol withdrawal symptoms and should not prompt treatment with benzodiazepines. Assess CIWA-A 5 hours after completion of the third phenobarbital intramuscular (IM) loading dose or 15 minutes after completion of the third phenobarbital intravenous (IV) loading dose. Reassessments should be repeated every 4 hours for the first 48 hours after initial phenobarbital loading. MD/LIP should be notified every time: - The CIWA score is > 10 - Confusion, agitation, or hallucinations - Somnolence/difficult to arouse - Respiratory depression

CIWA-A (step-down units)

Routine, CONTINUOUS Until Specified, Assess CIWA-A 5 hours after completion of the third phenobarbital intramuscular (IM) loading dose or 15 minutes after completion of the third phenobarbital intravenous (IV) loading dose. MD/LIP should be notified 1. Every time the CIWA-A score is >10. 2. Patient's CIWA-A score is still >10 after receiving the total phenobarbital loading dose. 3. Patients who become somnolent, difficult to arouse, or have respiratory depression.

MINDS (critical care areas, MICU step-down units)

Routine, CONTINUOUS Until Specified, Assess MINDS 5 hours after completion of the third phenobarbital intramuscular (IM) loading dose or 15 minutes after completion of the third phenobarbital intravenous (IV) loading dose. MD/LIP should be notified : 1. Every time the MINDS score is >10. 2. Patient's MINDS score is still >10 after receiving the total phenobarbital loading dose. 3. Patients who become somnolent, difficult to arouse, or have respiratory depression.

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Phenobarbital initial management (loading dose/maintenance regimen)

Patient has NOT received any benzodiazepine in last 12 hours

Patient received <20 mg lorazepam, 40 mg of midazolam, or 100 mg of diazepam in last 12 hours

PHENobarbital (LUMINAL) level - may be timed to be drawn 5 hours after the end of loading dose on day 1 (\$\$\$)

! PHENobarbital (LUMINAL) Loading Dose (Day 1)

Intramuscular route preferred, unless patient is acutely agitated, platelet <50,000 per microliter, INR >2 or therapeutically anticoagulated.

PHENobarbital (LUMINAL) IM Injection : 12 mg/kg total loading dose

PHENobarbital (LUMINAL) IV Push/IVPB : 12 mg/kg total loading dose

! Taper/Maintenance Dosing (Day 2-5)

PHENobarbital (LUMINAL) tablet : Day 2 - 5

PHENobarbital (LUMINAL) IM : Day 2 - 5

PHENobarbital (LUMINAL) IV Push/IVPB : Day 2 - 5

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Management of symptomatic patient who received phenobarbital loading dose (12 or 15 mg/kg)

- Patient received phenobarbital loading dose - 12 mg/kg
- Patient received cumulative phenobarbital loading dose - 15 mg/kg

Management of symptomatic patient who received phenobarbital loading dose (12 or 15 mg/kg)

Patient received phenobarbital loading dose - 12 mg/kg


PHENobarbital (LUMINAL) IM Injection

3 mg/kg (Ideal), Intramuscular, ONCE, Monitor blood pressure, heart rate, and respiratory status 15 minutes after dose administration, then every 2 hours while receiving loading dose, and re-check 2 hours after completion of the total loading dose. Hold therapy if blood pressure <90/50 mm Hg, heart rate <50 bpm, respiratory rate <10 bpm, RASS score <-2, or POSS <-1. Contact ordering provider to change loading dose to IV if patient is acutely agitated, platelet <50,000 per microliter, INR >2 or therapeutically anticoagulated. IM administration can be given in deltoid or gluteus muscles. Recommended maximum volumes for single IM injections are as follows. If the ordered volume exceeds the maximum recommended volume, split the ordered volume into multiple injections according to the following recommendations: Well-developed typical adult = 3 mL Thin or elderly adult = 2 mL Use ideal body weight (IBW) unless actual body weight is less than IBW then use actual body weight.

PHENobarbital (LUMINAL) IV Push/IVPB

3 mg/kg (Ideal), Intravenous, ONCE, Dilute doses \leq 260 mg with up to 10 mL of 0.9% sodium chloride or sterile water for injection. Administer intravenous doses \leq 260 mg as IV push at a rate of 60 mg/min. Monitor blood pressure, heart rate, and respiratory status 15 minutes after dose administration, then every 1 hour while receiving loading dose, and re-check 1 hour after completion of the total loading dose. Hold therapy if blood pressure <90/50 mm Hg, heart rate <50 bpm, respiratory rate <10 bpm, RASS score <-2, or POSS <-1. Use ideal body weight (IBW) unless actual body weight is less than IBW then use actual body weight.

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 Patient received cumulative phenobarbital loading dose - 15 mg/kg

May administer 2 mg/kg single doses every 3 hours for a total max of 25 mg/kg

PHENobarbital (LUMINAL) IM Injection

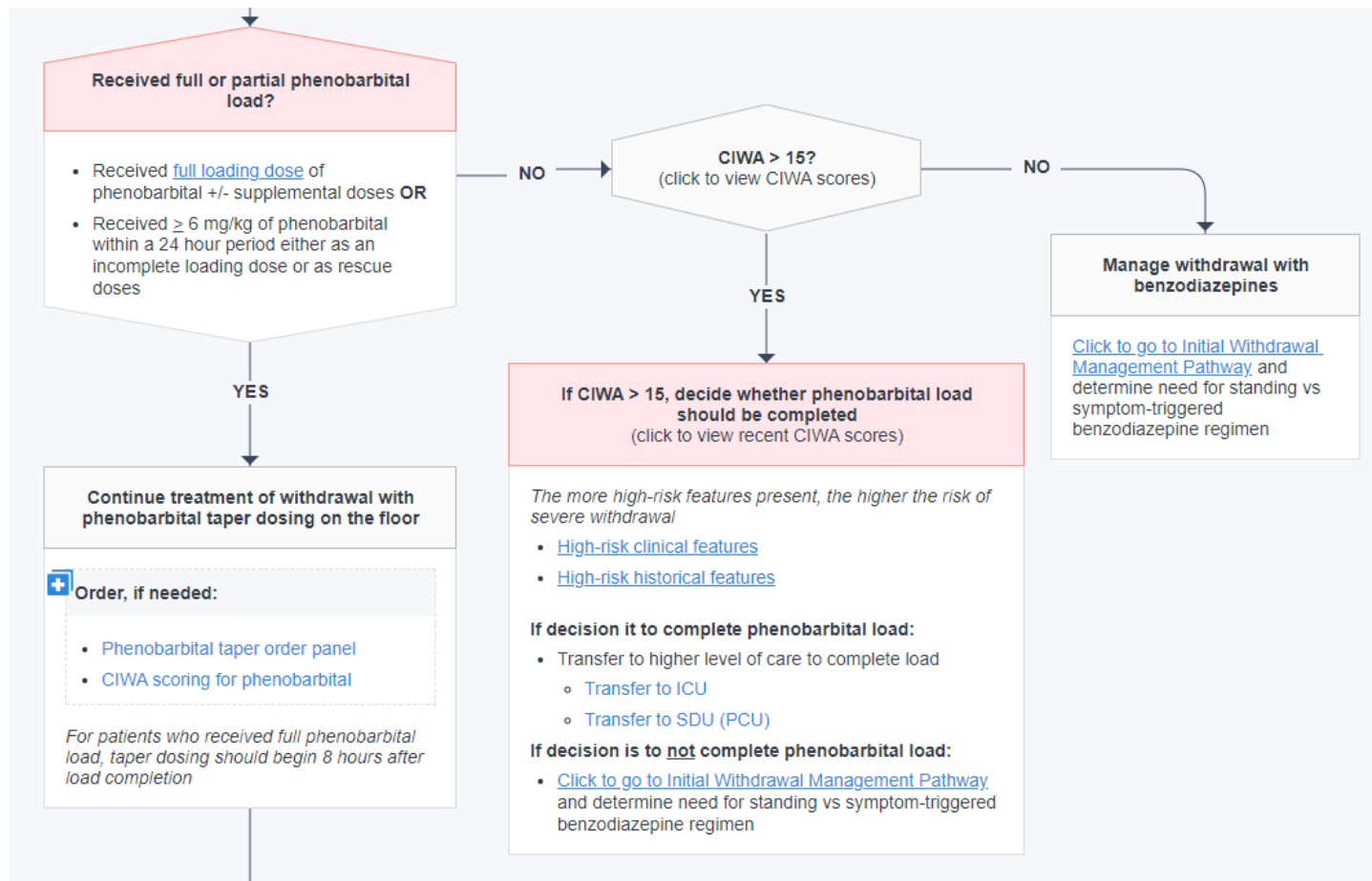
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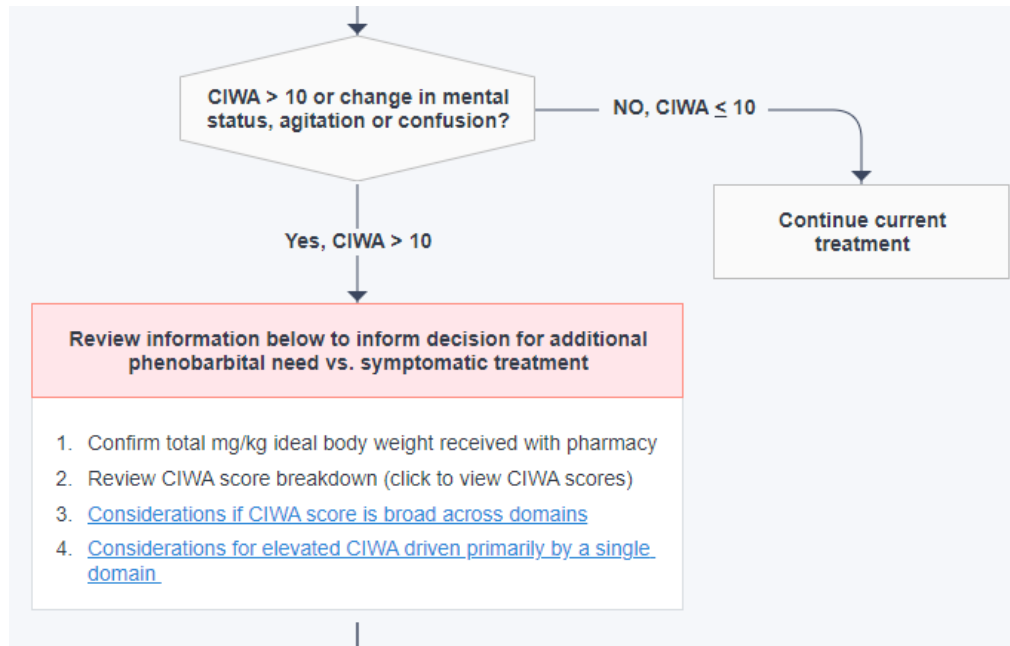
2 mg/kg (Ideal), Intravenous, ONCE, Dilute doses \leq 260 mg with up to 10 mL of 0.9% sodium chloride or sterile water for injection. Administer intravenous doses \leq 260 mg as IV push at a rate of 60 mg/min. Monitor blood pressure, heart rate, and respiratory status 15 minutes after dose administration, then every 1 hour while receiving loading dose, and re-check 1 hour after completion of the total loading dose. Hold therapy if blood pressure <90/50 mm Hg, heart rate <50 bpm, respiratory rate <10 bpm, RASS score <-2, or POSS <-1. Use ideal body weight (IBW) unless actual body weight is less than IBW then use actual body weight.

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Guidance for symptomatic patients who received full or partial phenobarbital load and are now being managed on the floor



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Considerations if CIWA score is broad across domains

If received ≥ 15 mg/kg of phenobarbital loading dose:

- 15 mg/kg of phenobarbital has been shown to be a sufficient dose in most patients to saturate GABA receptors and control alcohol withdrawal symptoms. Elevated CIWA may be due to other etiology; consider treatment of specific symptoms. If symptoms are felt due to escalating withdrawal, alternative ICU-level treatments or additional doses of phenobarbital are needed

If received < 15 mg/kg phenobarbital loading dose:

- Patient is more likely to benefit from receiving more phenobarbital

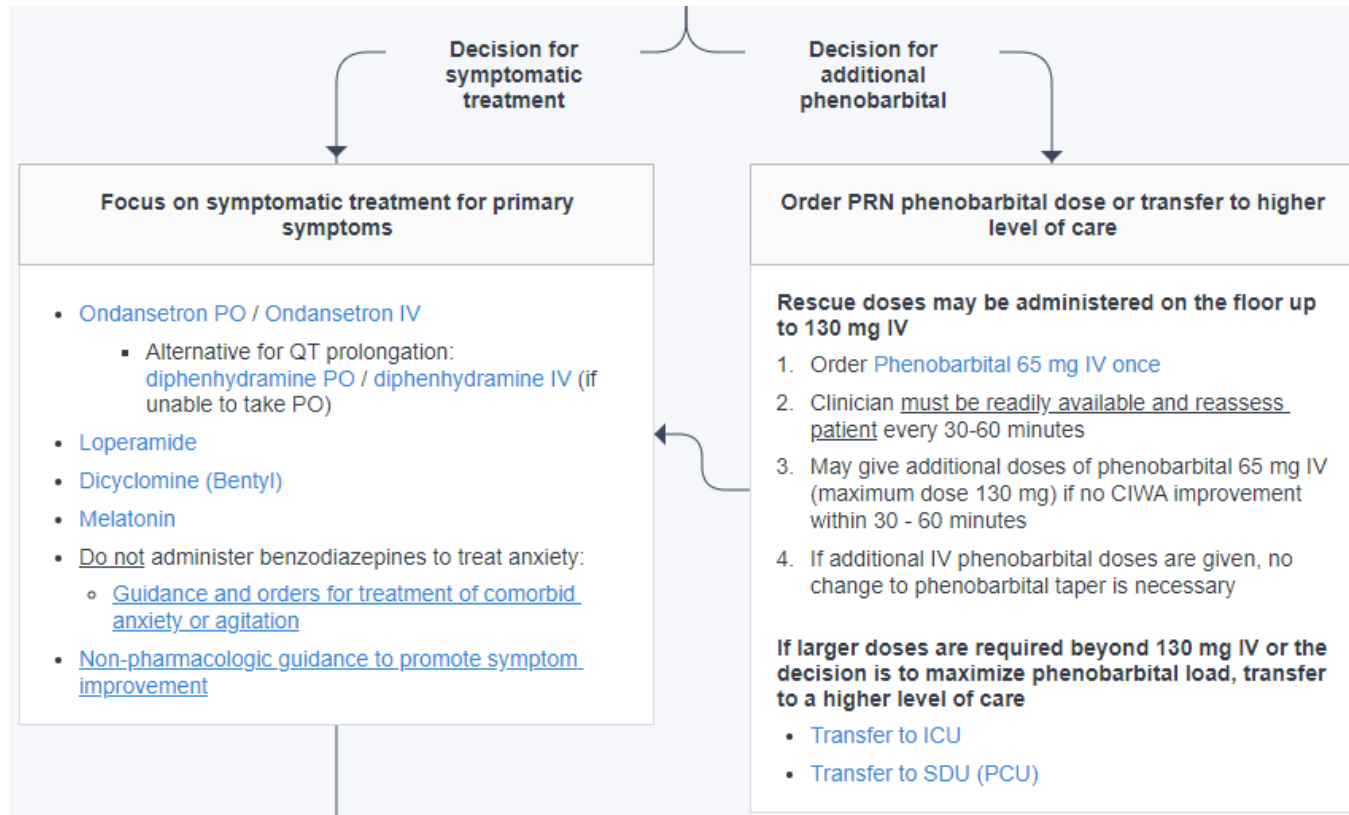
Additional patient-specific factors to consider:

- Withdrawing from additional substances?
- What are the patient's risk factors for severe withdrawal?
- How high is CIWA?
- Tachycardic? Hypertensive?
- Is CIWA trend stable, increasing, or decreasing?
 - May be appropriate to monitor vs administration of additional phenobarbital

Considerations for elevated CIWA driven by single domain

- Focusing on symptomatic treatment for primary symptoms with adjunctive medications may be appropriate

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Discontinuation of phenobarbital

- Due to long half-life, phenobarbital can be discontinued earlier in hospital course for patients no longer experiencing withdrawal symptoms
- Full 5-day admission to complete taper is not always necessary
- Phenobarbital should not be continued at discharge, including for patients leaving prematurely (AMA)
- Patients leaving prematurely should be warned about potential for increased alcohol toxicity due to increased alcohol sensitivity following phenobarbital therapy
- [Click here to go to AUD Treatment Initiation Pathway to initiate pharmacologic treatment for AUD](#)