Phenobarbital Loading

- Calculate target loading dose with phenobarbital depending on alcohol use severity and comorbid medical illness
- IBWt x (6 to 15mg/kg) = total mg
- Where:
  - IBWt for men is: 50 + 2.3 kg/inch over 5 feet.
  - IBWt for women is: 45.5 + 2.3kg/inch over 5 feet.
- Give loading dose intramuscularly:
  - 40% given immediately
  - 30% given 3 hours after 1st IM administration
  - 30% given 3 hours after 2nd IM administration

Phenobarbital Maintenance Dosing/Taper

- Day 3 is the same as day 2
- Day 4 the oral dose is decreased by 50%
- Day 5 it stays the same
- Day 6 decrease 50%
- Day 7 decrease 50%
- Then discontinue

- No benzodiazepines allowed and an order is placed that none can be given to the patient
  - No patient that received phenobarbital has received or required any benzodiazepines to date

Pharmacy & Therapeutics Guideline

Phenobarbital for Alcohol Withdrawal Syndrome in the Medical Intensive Care Unit

Purpose

To provide effective and safe guidelines on the use of phenobarbital for the treatment of alcohol withdrawal syndrome in the medical intensive care unit. Phenobarbital inhibits the N-methyl-D-aspartate (NMDA) receptor and activates the gamma-amino-butyric acid-A (GABA-A) receptor, yielding a useful pharmacologic mechanism for the management of severe alcohol withdrawal syndrome.[1]

Phenobarbital Loading Dose Management

STEP 1: Choose phenobarbital weight-based loading dose*

15 mG/kG (Divided into 3 doses given 3 hours apart)	20 mG/kG (Divided into 3 doses given 3 hours apart)
For patients meeting the following criteria: • Age > 65 years • AST/ALT > 3 times upper limit of normal	For patients who do not meet the 15 mG/kG criteria

* Additional/concurrent benzodiazepines are not recommended due to the risk of additive side effects
* If patients exhibit excessive sedation/somnolence, a portion of the loading dose may be withheld

STEP 2: How to order initial IV loading dose

- IV loading dose may be given **divided in 3 doses** (for most patients) or **one full dose** (if clinically warranted for severe withdrawal patients)
- Using **actual body weight**, dosing weight is **capped at 100 kG** (i.e., patients weighing > 100 kG, utilize the dosing regimen for 100 kG)
- If loading dose is divided in 3 doses, refer to **TABLE 1**
  - Enter order as 3 separate doses administered 3 hours apart using the alcohol withdrawal indication in Sunrise®
  - All doses > 130 mG must be entered as IVPB

Table 1: Initial Loading Doses*

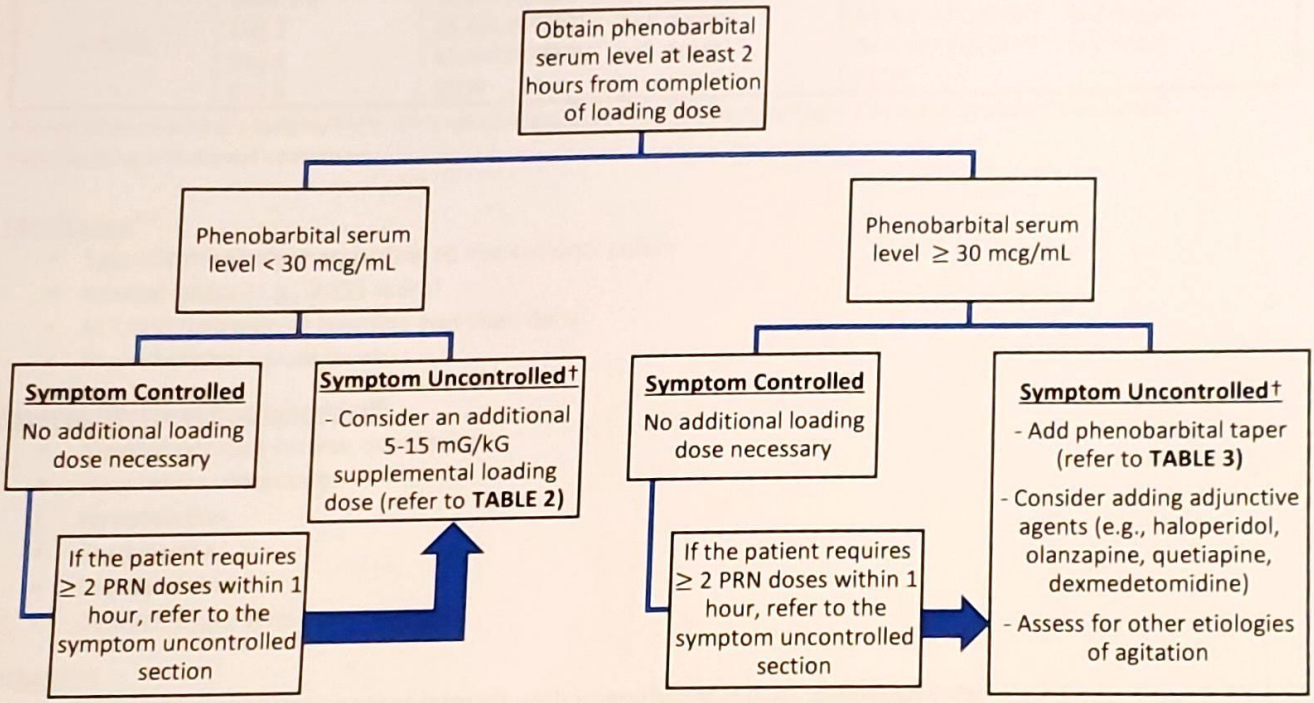
15 mG/kG				20 mG/kG			
Actual Body Weight (kG)	Dose 1 (mG)	Dose 2 (mG)	Dose 3 (mG)	Actual Body Weight (kG)	Dose 1 (mG)	Dose 2 (mG)	Dose 3 (mG)
45	260	260	130	45	390	260	260
50	390	260	130	50	390	260	260
55	390	260	130	55	520	260	260
60	390	260	260	60	520	390	260
65	390	260	260	65	520	390	390
70	520	260	260	70	650	390	390
75	520	390	260	75	650	390	390
80	520	390	260	80	650	520	390
85	520	390	390	85	780	520	390
90	520	390	390	90	780	520	520
95	650	390	390	95	780	520	520
100	650	520	390	100	780	650	520

* Phenobarbital doses ≤ 130 mG: administer as an IVP (no faster than 60 mG/minute)
* Phenobarbital doses > 130 mG: administer as an IVPB in 100 mL of 0.9% NaCl over 60 minutes
* For doses of 260 mG, may enter order as phenobarbital 130 mG IVP every 15 minutes (stop after 2 doses)

STEP 3: PRN for breakthrough agitation

- All patients require a phenobarbital IV push (IVP) order for breakthrough agitation
- Use Richmond Agitation Sedation Scale (RASS) to assess patient's mental status (see appendix)
- Enter order as: Phenobarbital 130 mg IVP every 15 minutes PRN for RASS ≥ 3 (stop after 4 doses)
  - Additional PRN orders for phenobarbital can be entered after reassessment by provider

Post-Loading Dose Management



†Symptom Uncontrolled = RASS ≥ 3

TABLE 2: Supplemental Loading Dose(s)

5 mG/kG		10 mG/kG			15 mG/kG			
Dosing Weight (kG)	Dose (mG)	Dosing Weight (kG)	Dose 1 (mG)	Dose 2 (mG)	Dosing Weight (kG)	Dose 1 (mG)	Dose 2 (mG)	Dose 3 (mG)
45	260	45	260	130	45	260	260	130
50	260	50	260	260	50	390	260	130
55	260	55	260	260	55	390	260	130
60	260	60	390	260	60	390	260	260
65	260	65	390	260	65	390	260	260
70	390	70	390	260	70	520	260	260
75	390	75	390	390	75	520	390	260
80	390	80	390	390	80	520	390	260
85	390	85	520	390	85	520	390	390
90	390	90	520	390	90	520	390	390
95	520	95	520	390	95	650	390	390
100	520	100	520	520	100	650	520	390

TABLE 3: Phenobarbital Taper†

Actual Body Weight	Taper Day	IV Taper Regimen	Oral Taper Regimen
≥ 70 kG	Days 1-2	130 mG IV Q8H (x 6 doses)	129.6 mG PO Q8H (x 6 doses)
	Days 3	130 mG IV Q12H (x 2 doses)	129.6 mG PO Q12H (x 2 doses)
	Day 4	130 mG IV Q24H (x 1 dose)	129.6 mG PO Q24H (x 1 dose)
	Day 5	**STOP**	**STOP**
< 70 kG	Days 1-2	65 mG IV Q8H (x 6 doses)	64.8 mG PO Q8H (x 6 doses)
	Day 3	65 mG IV Q12H (x 2 doses)	64.8 mG PO Q12H (x 2 doses)
	Day 4	65 mG IV Q24H (x 1 dose)	64.8 mG PO Q24H (x 1 dose)
	Day 5	**STOP**	**STOP**

†Given phenobarbital's long half-life, early discontinuation of phenobarbital taper can occur in patients no longer experiencing withdrawal symptoms

Monitoring[3,4]

- Episodic monitoring according to institutional policy
- Mental status (e.g., RASS score)
- ALT/AST/bilirubin at baseline and then daily
- Phenobarbital serum levels

Adverse Effects of Phenobarbital[2]

- Central nervous system depression
- Respiratory depression
- Hypotension
- Bradycardia
- Transaminitis
- Delayed hypersensitivity reactions

Exclusions

- On essential medications that interact with phenobarbital (e.g., antiretrovirals)
- Hepatic encephalopathy
- Chronic use of phenobarbital
- Pregnancy

References

1. Oks M, Cleven KL, Healy L, et al. The Safety and Utility of Phenobarbital Use for the Treatment of Severe Alcohol Withdrawal Syndrome in the Medical Intensive Care Unit. *Journal of Intensive Care Medicine*. 2018;35(9):844-850.
2. Phenobarbital [package insert]. Berkeley Heights, NJ: Hikma Pharmaceuticals USA Inc; 2020.
3. Northwell Health. LIJMC Intravenous (IV) Medication General Reference Guide. January 2023.
4. Northwell Health. North Shore University Hospital Adult Intravenous Administration Reference. March 2023.