



UW PACC

Psychiatry and Addictions Case Conference

UW Medicine | Psychiatry and Behavioral Sciences

SHOULD I USE BENZODIAZEPINES FOR AMBULATORY ALCOHOL WITHDRAWAL MANAGEMENT?

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SPEAKER DISCLOSURES

✓ No conflicts of interest

PLANNER DISCLOSURES

The following series planners have no relevant conflicts of interest to disclose; other disclosures have been mitigated.

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OBJECTIVES

1. Understand the importance of treatment of alcohol withdrawal
2. Identify which patients are appropriate for ambulatory management of alcohol withdrawal
3. Learn different pharmacologic strategies for ambulatory withdrawal management
4. Understand proper use of benzodiazepines for ambulatory treatment, and the risks involved

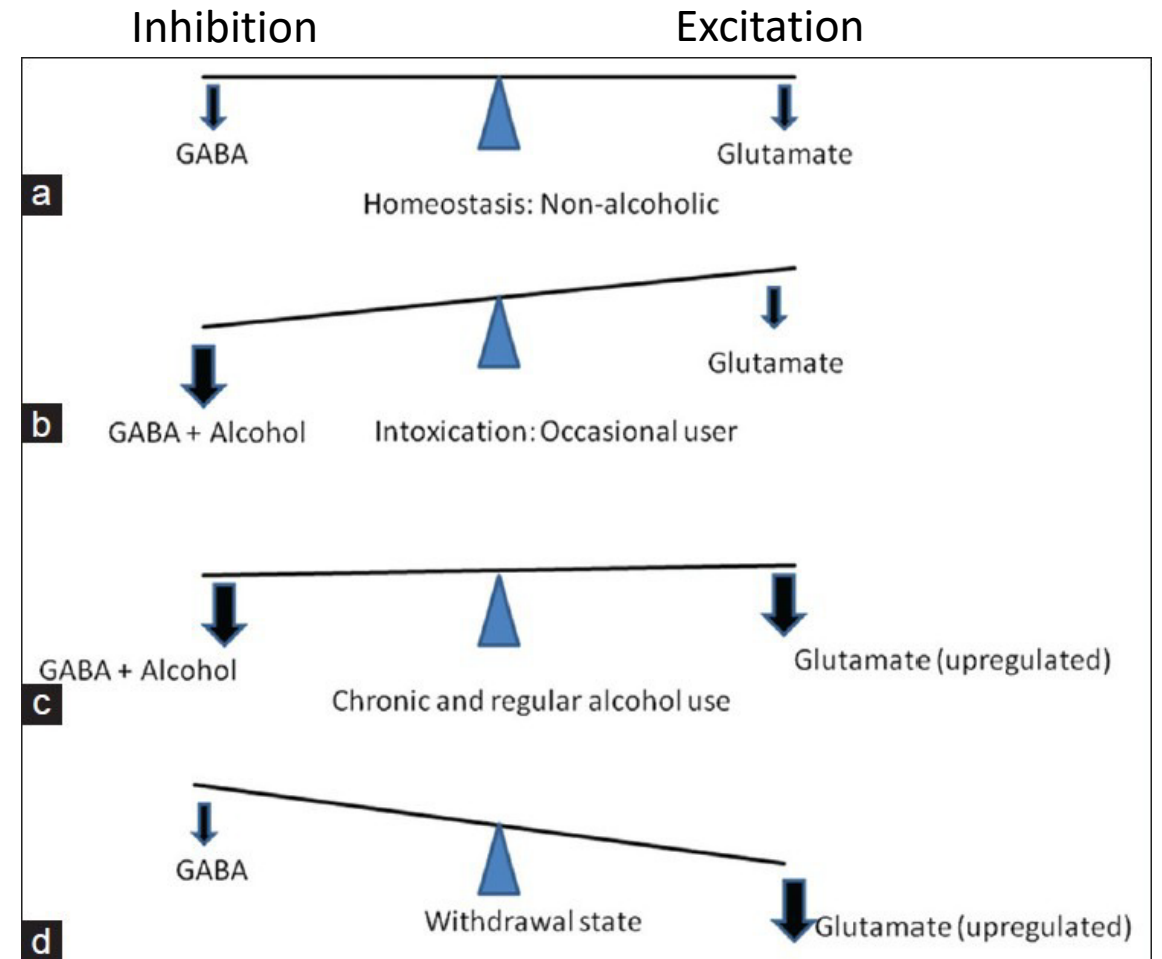
ALCOHOL WITHDRAWAL

- Abrupt cessation or reduction of alcohol after a prolonged period of heavy use
- 2+ of the following symptoms:
 - Autonomic hyperactivity
 - Increased hand tremor
 - Insomnia
 - Nausea, Vomiting
 - Hallucinations/Illusions
 - Psychomotor Agitation
 - Anxiety
 - Seizures



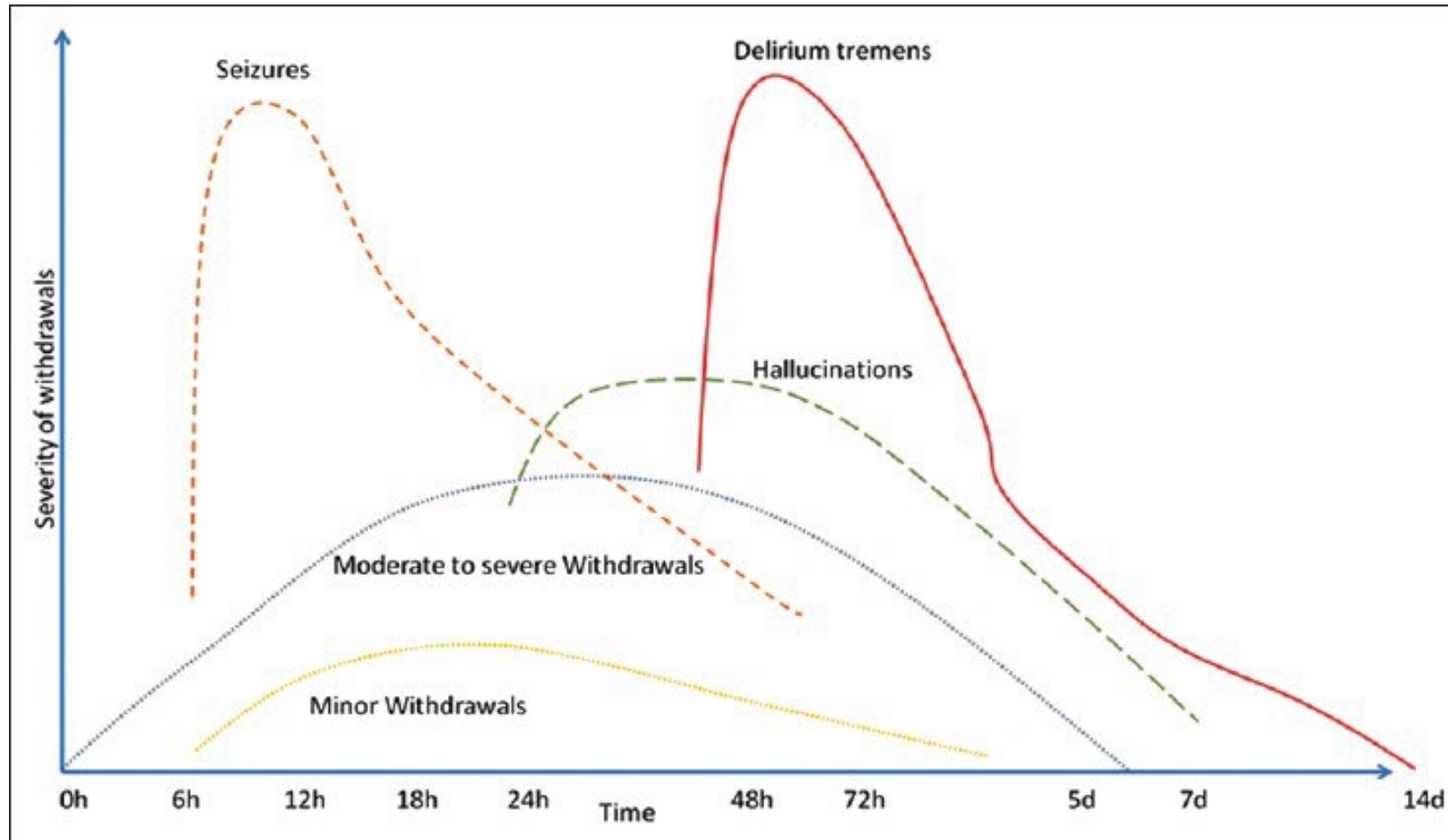
ALCOHOL WITHDRAWAL

- Alcohol acts as “inhibitor”
- Chronic use resets balance of inhibition and excitation
- Withdrawal is result of “unmasking” of skewed balance when alcohol removed



Kattimani, 2013

ALCOHOL WITHDRAWAL TIMELINE



Kattimani, 2013

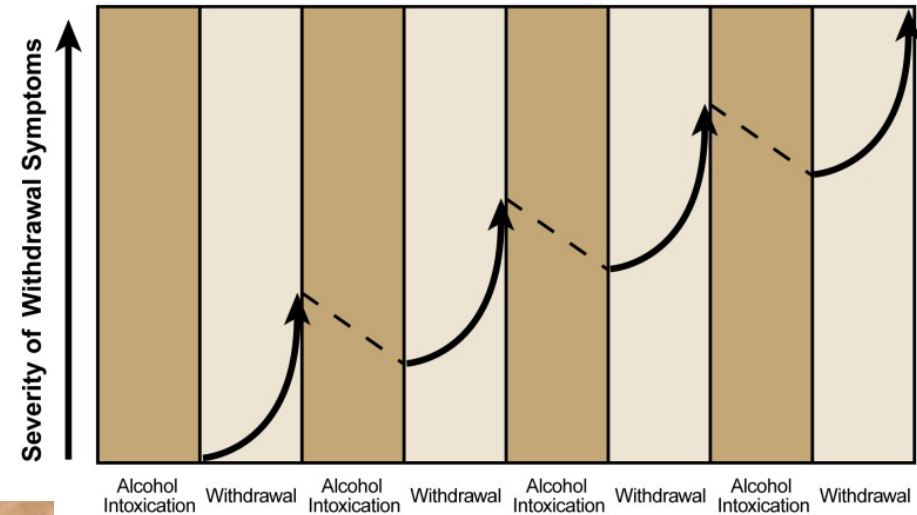
WHY TREAT ALCOHOL WITHDRAWAL?

- Patient comfort
 - Increased abstinence
- Serious/life threatening symptoms
 - Seizures
 - Hallucinosiis
 - Delirium Tremens

WHY TREAT ALCOHOL WITHDRAWAL?

Kindling effect:

- First observed in epilepsy
- Periods of withdrawal →
Hyperexcitability of the Central Nervous System (CNS) →
Persistent CNS hyperexcitability →
More intense withdrawal sx



Repeated Cycles of Alcohol Intoxication and Withdrawal

Becker, 1998

AMBULATORY WITHDRAWAL MANAGEMENT

Process of detoxing down or off alcohol in an **outpatient** setting



AMBULATORY WITHDRAWAL MANAGEMENT

Pros:

- Patients can remain at home, work, etc.
- More autonomy (self-evaluation and self-management)
- Lower cost on healthcare system
- Shorter time of treatment?

Cons:

- Less monitoring
- Fewer medication options, routes of administration
- No guarantee of follow-up

WHO DOESN'T GET TO DO AMBULATORY WITHDRAWAL?

- Contraindications:
 - Hx of withdrawal delirium (OR 2.6 of recurrent delirium)
 - Hx of withdrawal seizures (OR 2.8 of recurrent seizure)
 - Severe withdrawal (CIWA > 15)
 - Inability to take oral medications
 - Complex medical or psychiatric comorbidities:
 - Heart Failure
 - Kidney Disease
 - Uncontrolled diabetes
 - Recent Head Injury (risk of increased cranial pressure)
 - Active psychosis, mania, severe depression/SI
 - Benzodiazepine use disorder
 - Pregnancy



OTHER CONSIDERATIONS FOR INPATIENT TREATMENT

- Social situation:
 - Unhoused/unstable living environment
 - Lack of reliable transportation
 - Lack of social support to aid in monitoring
- Cognitive limitations
 - Difficulty with remembering appointments, self-directing treatment
 - Difficulty reporting history accurately

CIWA

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

Nausea and vomiting	Headache
0: No nausea or vomiting	0: Not present
1	1: Very mild
2	2: Mild
3	3: Moderate
4: Intermittent nausea with dry heaves	4: Moderately severe
5	5: Severe
6	6: Very severe
7: Constant nausea, frequent dry heaves and vomiting	7: Extremely severe
Paroxysmal sweats	Auditory disturbances
0: No sweats visible	0: Not present
1: Barely perceptible sweating, palms moist	1: Very mild harshness or ability to frighten
2	2: Mild harshness or ability to frighten
3	3: Moderate harshness or ability to frighten
4: Beads of sweat obvious on forehead	4: Moderately severe hallucinations
5	5: Severe hallucinations
6	6: Extremely severe hallucinations
7: Drenching sweats	7: Continuous hallucinations
Anxiety	Visual disturbances
0: No anxiety, at ease	0: Not present
1	1: Very mild photosensitivity
2	2: Mild photosensitivity
3	3: Moderate photosensitivity
4: Moderately anxious, guarded	4: Moderately severe visual hallucinations
5	5: Severe visual hallucinations
6	6: Extremely severe visual hallucinations
7: Acute panic state, consistent with severe delirium or acute schizophrenia	7: Continuous visual hallucinations
Agitation	Tactile disturbances
0: Normal activity	0: None
1: Somewhat more than normal activity	1: Very mild paresthesias
2	2: Mild paresthesias
3	3: Moderate paresthesias
4: Moderately fidgety and restless	4: Moderately severe hallucinations
5	5: Severe hallucinations
6	6: Extremely severe hallucinations
7: Paces back and forth during most of the interview or constantly thrashes about	7: Continuous hallucinations
Tremor	Orientation and clouding of sensorium
0: No tremor	0: Oriented and can do serial additions
1: Not visible, but can be felt at fingertips	1: Cannot do serial additions
2	2: Disoriented for date by no more than 2 calendar days
3	3: Disoriented for date by more than 2 calendar days
4: Moderate when patient's hands extended	4: Disoriented for place and/or patient
5	
6	
7: Severe, even with arms not extended	
	Total score is a simple sum of each item score (maximum score is 67)
	Score:
	<10: Very mild withdrawal
	10 to 15: Mild withdrawal
	16 to 20: Modest withdrawal
	>20: Severe withdrawal

Adapted from Sullivan JT, Skjora K, Schneiderman J, et al. Br J Addict 1989; 84:1353.

UpToDate®

Total score is a simple sum of each item score (maximum score is 67)

Score:

<10: Very mild withdrawal

10 to 15: Mild withdrawal

16 to 20: Modest withdrawal

>20: Severe withdrawal

ASAM:

<10: Mild

10-18: Moderate

19+: Severe

REGIMENS FOR AMBULATORY WITHDRAWAL

- Fixed dose vs Symptom-Triggered
- Fixed dose is recommended for outpatient
 - Avoids “missing” the first seizure
 - Less subjectivity for pt
 - More risk for overdosing and underdosing
 - Instruct to hold doses for oversedation, resume at original schedule (no makeup needed for missed doses)
 - Can provide as needed supply for breakthrough symptoms
- Generally, medication is initiated when they wake, prior to consuming any alcohol

REGIMENS FOR AMBULATORY WITHDRAWAL

- Caveat: protocols can vary widely depending on institution!
 - Available/allowed medications
 - Adopted dosing strategies
 - Published regimens have range recommendations
 - Individual provider perceptions

MEDICATIONS FOR AMBULATORY WITHDRAWAL

Mild Withdrawal (CIWA <10) : **Gabapentin**

Fixed Dose Schedule:

Day 1: 300mg every 6 hours (1200mg)

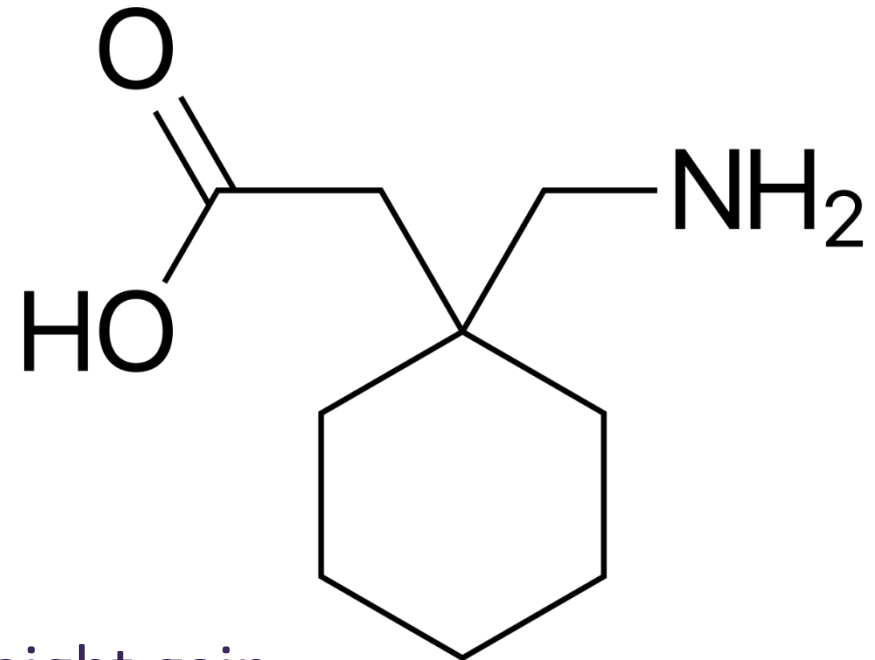
Day 2: 300mg every 8 hours (900mg)

Day 3: 300mg every 12 hours (600mg)

Day 4: 300mg once at bedtime (300mg)

+ 5 add'l doses as needed

Adverse effects: Sedation, dizziness, ataxia, weight gain



MEDICATIONS FOR AMBULATORY WITHDRAWAL

Mild Withdrawal (CIWA <10) : **Gabapentin**

*Can be continued after acute withdrawal

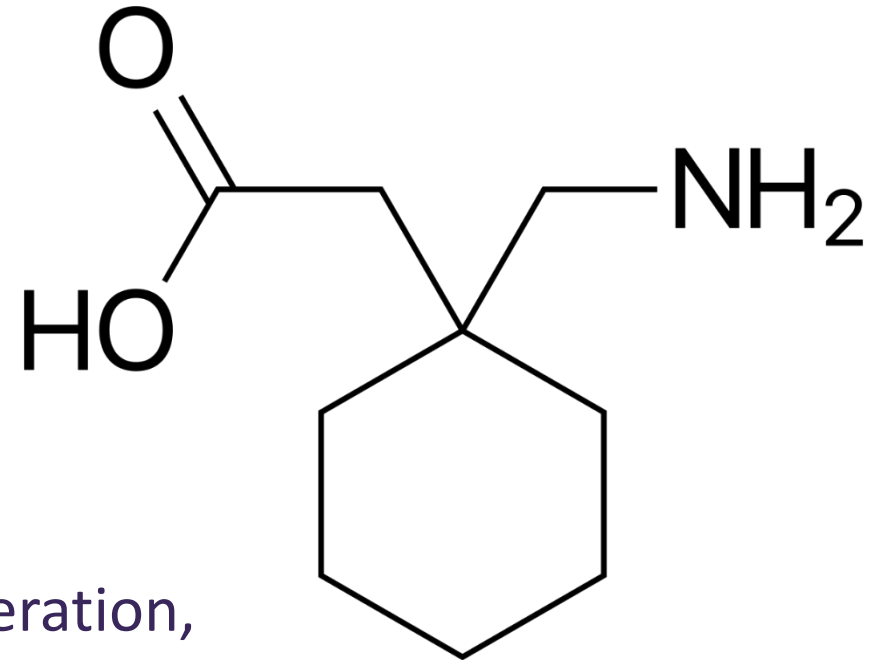
Helps with protracted withdrawal:

Alcohol cravings

Anxiety

Sleep

*also appropriate for patients whose goal is moderation,
not abstinence



MEDICATIONS FOR AMBULATORY WITHDRAWAL

- Gabapentin titration for continued use after acute withdrawal:
Seattle VA ATC
 - Day 1: 300mg TID (900mg)
 - Day 2: 600mg TID (1800mg)
 - Day 3+: Continue at 600mg TID if tolerated

MEDICATIONS FOR AMBULATORY WITHDRAWAL

Mild Withdrawal (CIWA <10) : **Carbamazepine**

Fixed Dose Schedule:

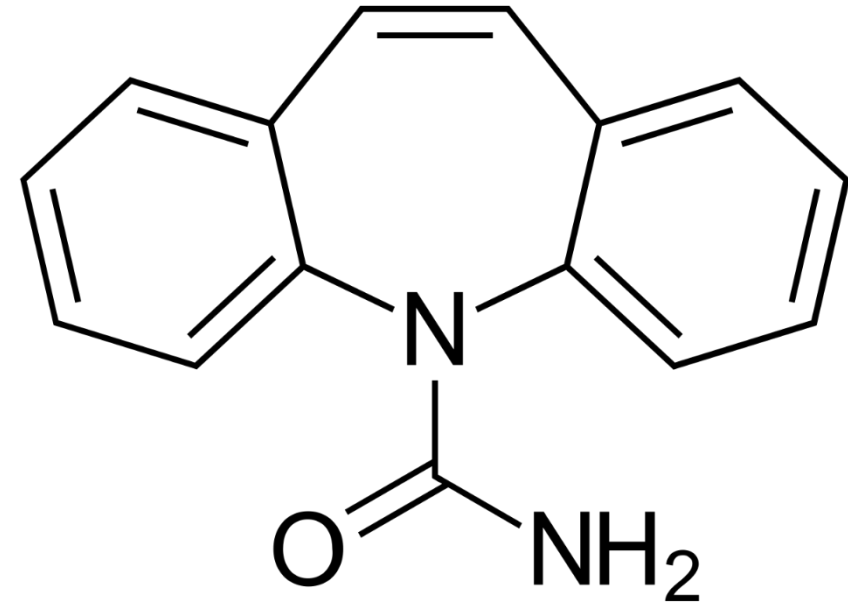
Day 1: 200mg every 6 hours (800mg)

Day 2: 200mg every 3 hours (600mg)

Day 3: 200mg every 12 hours (400mg)

Day 4: 200mg once at bedtime (200mg)

+ 5 add'l doses as needed

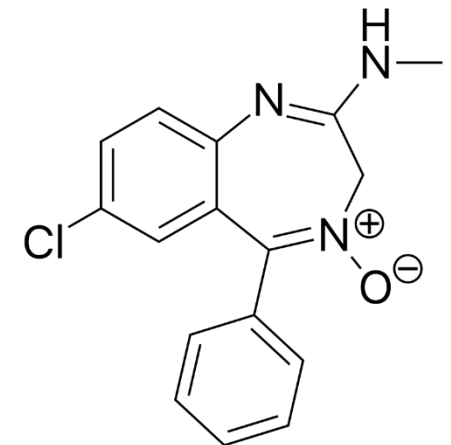
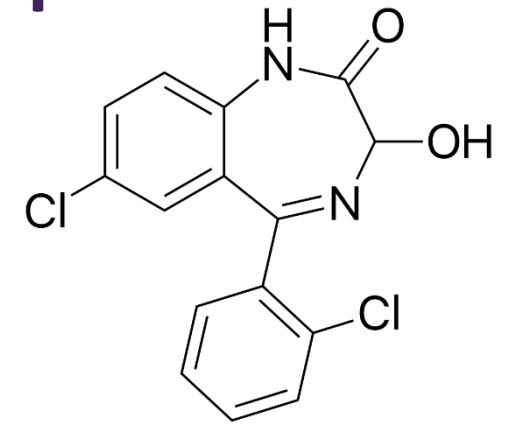
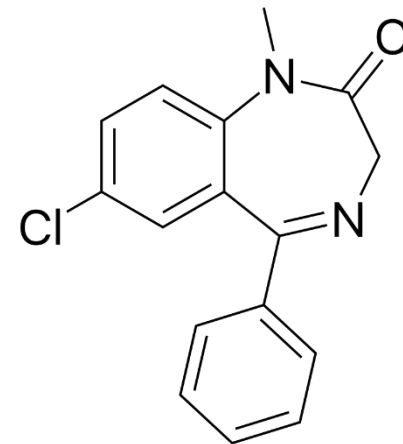


Adverse effects: sedation, dizziness, nausea, rash (SJS), SAIDH, agranulocytosis

*Metabolism can be an issue: auto-metabolism and CYP induction -> lower efficacy of other drugs

MEDICATIONS FOR AMBULATORY WITHDRAWAL

- Moderate withdrawal (CIWA 10-15) : **Benzodiazepines**
- Which one?
 - Longer-acting is better
 - More “even, steady” effect
 - Self-tapering
 - Lower risk of misuse



LORAZEPAM VS CHLORDIAZEPOXIDE VS DIAZEPAM

Generic name	Trade name	Usual single adult dose (oral)	Oral peak (hours)	Half-life (hours) parent	Metabolite activity*	CYP3A4 interactions [†]
Intermediate-acting (12 to 24 hours)						
Alprazolam	Xanax	0.25 to 0.5 mg	1 to 2	6 to 27	Inactive	Yes
Bromazepam ^Δ	Lexotan, Lexotanil	2 to 6 mg	1 to 2	8 to 20	Inactive	Limited
Estazolam	Prosom	0.5 to 2 mg	0.5 to 6	10 to 24	Inactive	Limited
Etizolam ^{Δ◇}	Depas, Etilaam, Etizola	0.5 to 1 mg	0.5 to 3	3 to 6	Active (half-life 8 hours)	Yes
Lorazepam	Ativan	0.5 to 3 mg	2 to 4	10 to 20	Inactive	No
Oxazepam	Serax	10 to 30 mg	2 to 4	5 to 20	Inactive	No
Temazepam	Restoril	7.5 to 30 mg	1 to 2	3 to 19	Inactive	No
Long-acting (>24 hours)						
Chlordiazepoxide	Librium	5 to 25 mg	0.5 to 4	5 to 30	Active	Yes (CYP3A4 inhibitors); limited (CYP3A4 inducers)
Clobazam	Onfi	10 to 20 mg	0.5 to 4	36 to 42	Active (half-life 71 to 82 hours)	Limited (interacts via CYP2C19)
Clonazepam	Klonopin	0.25 to 0.5 mg	1 to 2	18 to 50	Inactive	Limited
Clorazepate	Tranxene	7.5 to 15 mg	1 to 2	Prodrug	Active (half-life 20 to 160 hours)	Limited
Diazepam	Valium	2 to 10 mg	0.5 to 1	20 to 50	Active	Yes (also interacts via CYP2C19)
Flunitrazepam ^Δ	Rohypnol	0.5 to 2 mg	1 to 2	16 to 35	Active	Limited
Flurazepam	Dalmane	15 to 30 mg	0.5 to 1	2 to 4	Active	Limited

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BENZODIAZEPINE METABOLISM

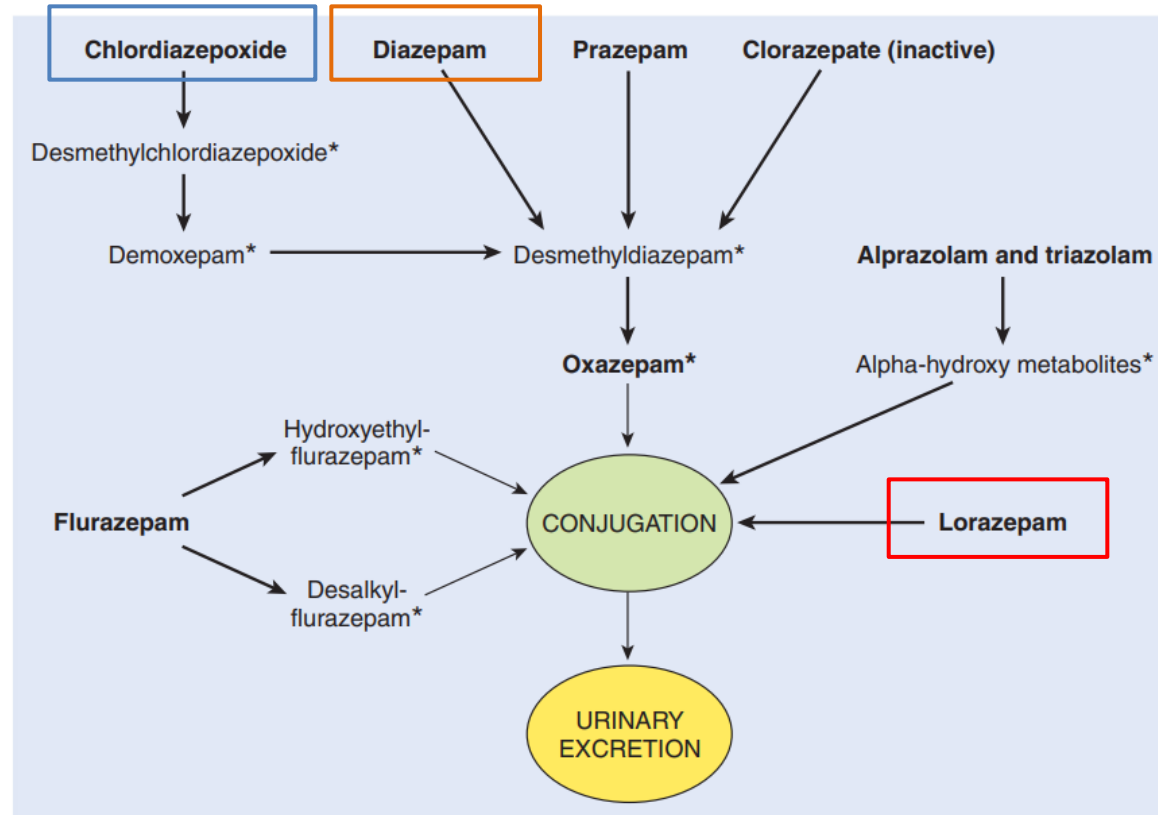
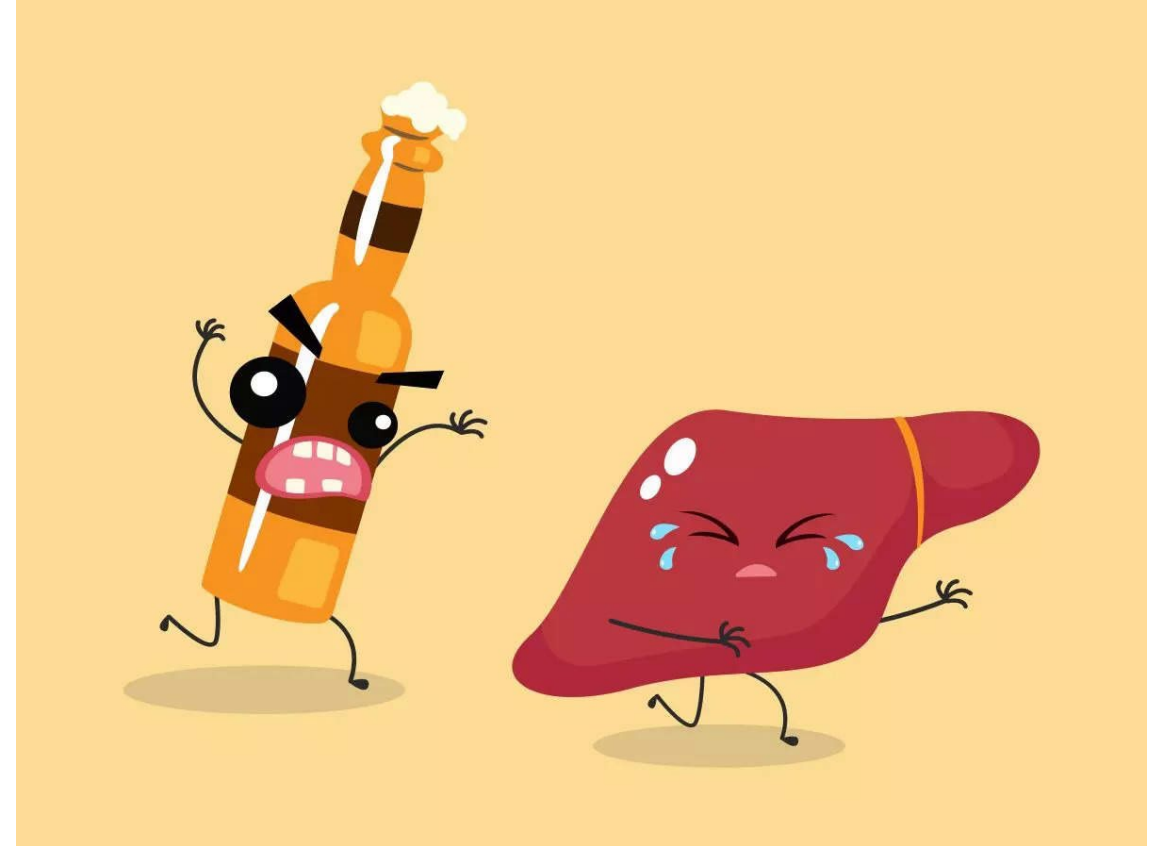


FIGURE 22-5 Biotransformation of benzodiazepines. (Boldface, drugs available for clinical use in various countries; *, active metabolite.)

Katzung, 2012

BENZODIAZEPINE METABOLISM

- Consider lorazepam if:
 - LFTs elevated more than 5x upper limit of normal
 - $AST > 185$
 - $ALT > 195$
 - Hx of cirrhosis or other severe liver disease
 - Previous adverse reaction to other benzos
 - You don't have information about liver function



DOSING OF BENZODIAZEPINES FOR WITHDRAWAL

- **Chlordiazepoxide**

- Day 1: 50mg every 6 hours (200mg)
- Day 2: 50mg every 8 hours (150mg)
- Day 3: 50mg every 12 hours (100mg)
- Day 4: 50mg at bedtime (50mg)
- + 5 doses for as needed

- **Diazepam**

- Day 1: 10mg every 6 hours (40mg)
- Day 2: 10mg every 8 hours (30mg)
- Day 3: 10mg every 12 hours (20mg)
- Day 4: 10mg at bedtime (10mg)
- + 5 doses for as needed

- **Lorazepam (AAFP)**

- 0.5-1mg every 6-8 hours for 3-5 days
- + 1mg every 4 hours as needed

- **ASAM: Taper by 25-50% daily over 3-5 days**



Holt SR and JM Tetrault. Alcohol withdrawal: Ambulatory management. In: UpToDate, Connor RF (Ed), Wolters Kluwer. (Accessed on Feb 11 2025.)

The ASAM Clinical Practice Guideline on Alcohol Withdrawal Management. J Addict Med. 2020 May/Jun;14(3S Suppl 1):1-72. doi: 10.1097/ADM.0000000000000668.

Erratum in: J Addict Med. 2020 Sep/Oct;14(5):e280. doi: 10.1097/ADM.0000000000000731. PMID: 32511109.

Tiglao SM, Meisenheimer ES, Oh RC. Alcohol Withdrawal Syndrome: Outpatient Management. Am Fam Physician. 2021 Sep 1;104(3):253-262. PMID: 34523874.

DOSING OF BENZODIAZEPINES FOR WITHDRAWAL

- **Seattle VA ATC:**

- **Chlordiazepoxide**

- Day 1: 50mg every 6 hours (200mg)
 - Day 2: 25mg TID (75mg)
 - Day 3: 25mg BID (50mg)
 - Day 4: 25mg daily (25mg)

- **Lorazepam**

- Day 1: 2mg TID (6mg)
 - Day 2: 2mg BID (4mg)
 - Day 3: 1mg BID (2mg)
 - Day 4: 0.5mg BID (1mg)



BENZOS AS ADJUNCT

- Seattle VA ATC:
 - Can give prn lorazepam for breakthrough withdrawal symptoms WITH gabapentin
 - 1mg q6h prn, up to #10
 - For pts who have had anxiety be a large component of previous attempts
 - Benzos have helped in the past but they do not currently meet criteria for moderate withdrawal

RISKS OF BENZODIAZEPINES

- Dependence
- Misuse
 - Diversion
- Withdrawal
- Adverse side effects: Especially when combined with alcohol!
 - Respiratory Depression -> Death
 - Sedation
 - Confusion
 - Delirium
 - Falls

CORRELATION WITH AUD

- Ciraulo et al. 1988: Literature review re: Benzo Abuse Among Alcoholics
 - Conclusion: “There is a body of literature which suggests that alcoholics as a group **may be more susceptible** to benzodiazepine abuse than are nonalcoholics, but there **is little evidence to suggest that all or even** most alcoholics abuse them”
 - “We feel that benzodiazepines are relatively safe drugs with many uses in the treatment of alcoholics when **prescribed rationally**”
 - Diagnostic/indication clarity
 - Involving nonmedication therapies
 - Using medications with less dependency potential
 - Limiting amounts of pills prescribed
 - Careful follow up including drug screening

CORRELATION WITH AUD

- Hirschtritt et al, 2019: Analysis of characteristics of patients with unhealthy alcohol use who used benzodiazepines in primary care setting
 - Results: Benzo use associated with:
 - Alcohol use disorder
 - Women
 - Older age
 - White race
 - Lower SES
- McHugh et al, 2021: Survey re: Benzo Misuse in AUD
 - 50% of participants reported past benzo use
 - 30% of participants reported past benzo misuse
 - Most common reason for misuse was coping
 - Demographics associated with misuse:
 - Younger Age
 - Female Sex
 - Anxiety
 - Other substance use
 - Conclusion: Benzodiazepine misuse is fairly common among people with AUD, untreated psychiatric symptoms may contribute to misuse

Hirschtritt ME, Palzes VA, Kline-Simon AH, Kroenke K, Campbell CI, Sterling SA. Benzodiazepine and unhealthy alcohol use among adult outpatients. *Am J Manag Care.* 2019 Dec 1;25(12):e358-e365. PMID: 31860229; PMCID: PMC7217068.

McHugh RK, Votaw VR, Taghian NR, Griffin ML, Weiss RD. Benzodiazepine misuse in adults with alcohol use disorder: Prevalence, motives and patterns of use. *J Subst Abuse Treat.* 2020 Oct;117:108061. doi: 10.1016/j.jsat.2020.108061. Epub 2020 Jun 22. PMID: 32811622; PMCID: PMC7438601.

GABAPENTIN FOR MODERATE WITHDRAWAL

- Myrick et al, 2009: Comparing gabapentin vs lorazepam for outpatient withdrawal
 - Gabapentin (1200mg or 900mg daily) or lorazepam (6mg daily) for 4 days
 - CIWA 10 or above
 - During Treatment:
 - CIWA scores decreased in all groups, no major clinical differences
 - lorazepam group was more likely to return to alcohol use
 - After treatment:
 - gabapentin group less likely to return to alcohol use
 - Overall:
 - Gabapentin 1200mg group had less anxiety, sedation, cravings
 - *600mg gabapentin group → 3 adverse events (2 seizures and 1 syncope)
 - Insufficient dose → start with at least 900mg daily dose

COMPARING GABAPENTIN WITH CHLORDIAZEPOXIDE

- Stock et al, 2013: Comparing gabapentin vs chlordiazepoxide for outpatient withdrawal
 - Veterans with CIWA 5 or above but not requiring hospitalization
 - Results:
 - Sleepiness and cravings scores were **lower** for gabapentin group in later treatment
 - No significant difference in CIWA scores between groups → gabapentin is as effective for sx of withdrawal!

Day	Gabapentin	Chlordiazepoxide
1	1200mg	100mg
2	1200mg	100mg
3	1200mg	100mg
4	900mg	75mg
5	600mg	50mg
6	300mg	25mg

ADJUNCTIVE THERAPY FOR ALCOHOL WITHDRAWAL

- **Beta Blockers:** for hypertension, tachycardia
 - Atenolol: 25-30mg daily
 - Metoprolol: 25-50mg every 12 hours
- **Clonidine:** for autonomic hyperactivity or anxiety
 - 0.1mg every 12 hours
- **Antiemetics:** for nausea/vomiting
 - Ondansetron 4mg every 8 hours
- **Nutritional support**
 - Folate 1mg daily
 - Thiamine 100mg daily
- **Valproic Acid:** for agitation, with or without other antiepileptics
 - 300-500mg every 6-8 hours

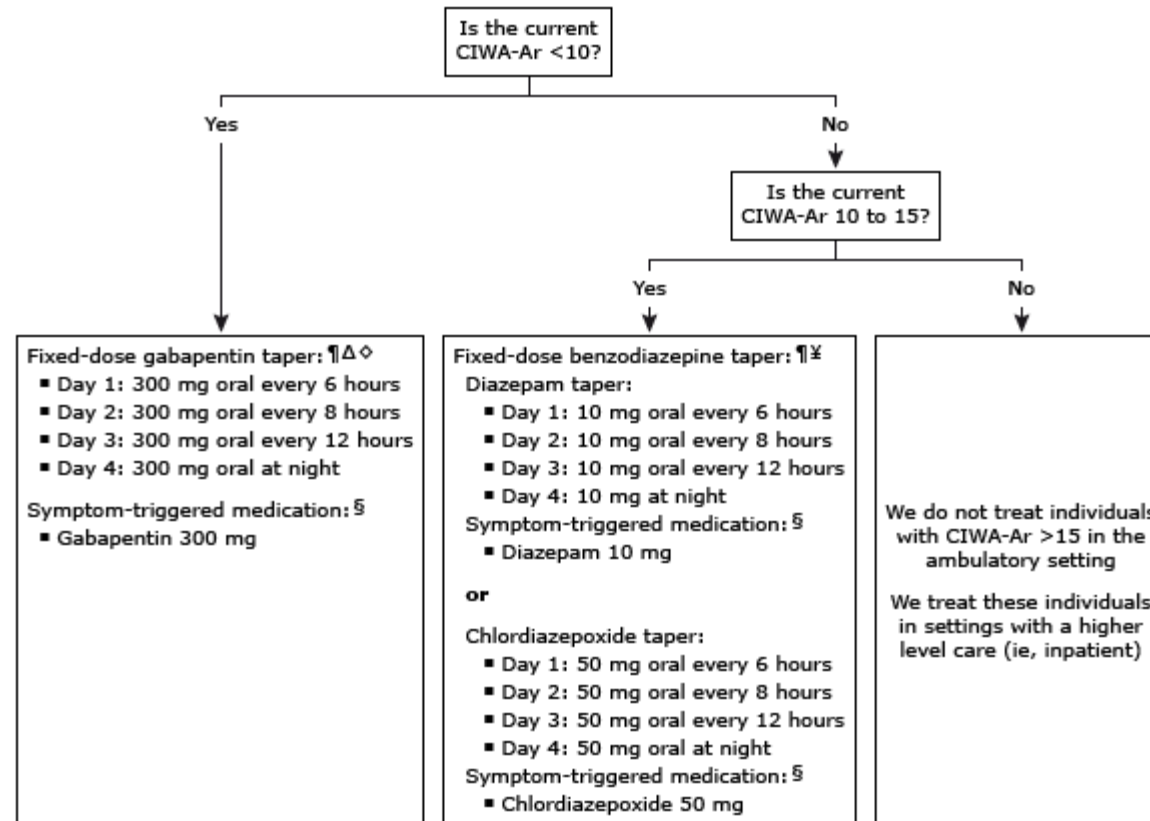
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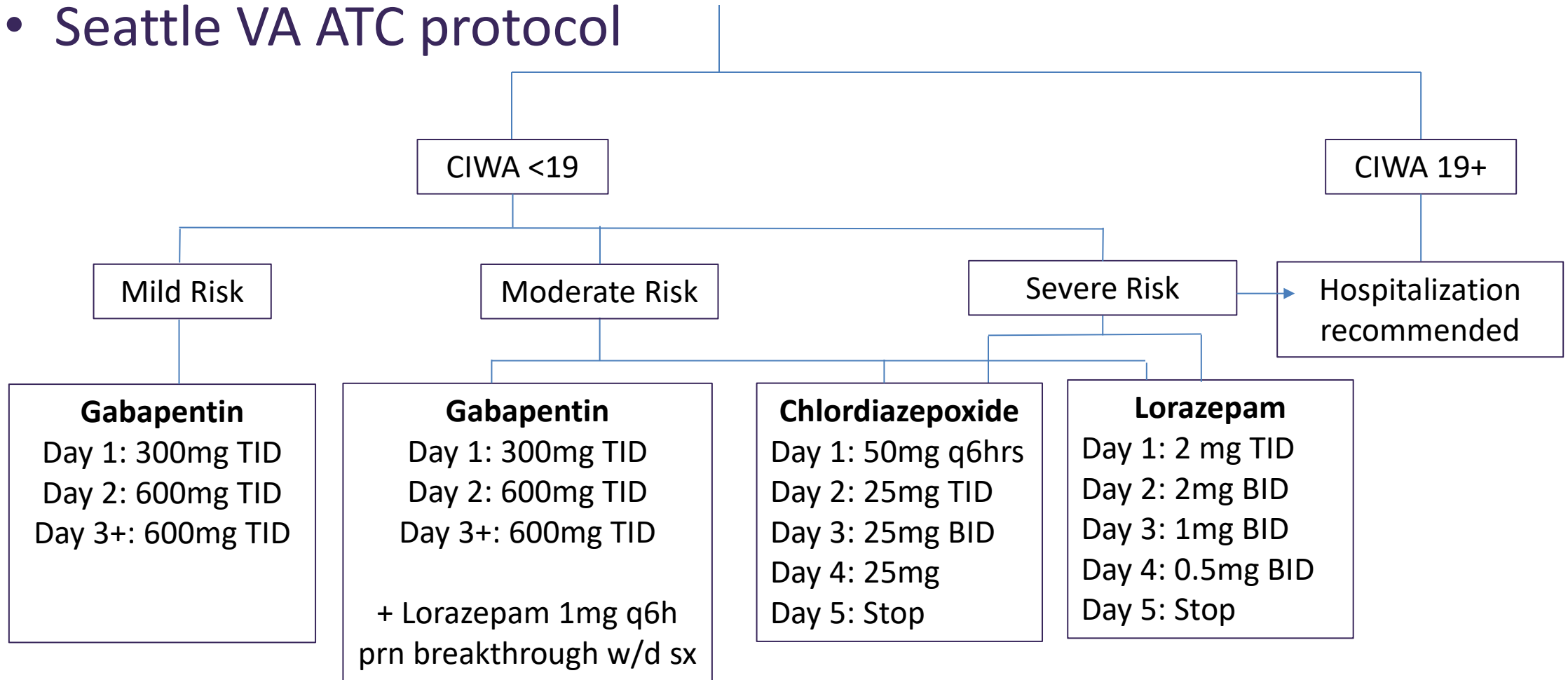
SUMMARY OF MEDICATIONS FOR WITHDRAWAL



Or carbamazepine

SUMMARY OF MEDICATIONS FOR WITHDRAWAL

- Seattle VA ATC protocol



OTHER PEARLS FOR OUTPATIENT MANAGEMENT

- Recruit help of a family/household member
 - If pt is at risk for incorrectly taking medication, ask support to supervise/administer medication
- Review their options in case outpatient plan isn't tolerable
 - Scheduled inpatient detox
 - ED for emergent admission
 - Criteria to look out for
 - CIWA scale



OTHER PEARLS FOR OUTPATIENT MANAGEMENT

- **Avoid detox** if high likelihood of imminent return to use
 - More episodes of withdrawal → Kindling effect
 - Avoid prescribing benzos due to risk of lethality with alcohol
 - Wait until there is an established aftercare plan (outpatient, IOP, residential)
 - Can encourage cutting down on alcohol rather than complete stop



FOLLOW UP CARE

- Close follow up for 3+ days following initiation of treatment
 - +/- starting before a (long) weekend
 - Assess symptoms
 - Assess how much scheduled medication and prns have been used
 - Utilize support staff (RNs, MAs)
 - Telehealth options



PATIENT CASE

PATIENT CASE

- 45 year old housed, employed, married man with history of alcohol use, reporting recent increase in alcohol consumption over the past several months, with several unsuccessful attempts to quit/cut down due to experiencing anxiety, insomnia, and mild perceptual disturbances. Recently using half of a fifth of gin daily (8-9 drinks) but reduced to 4 drinks/day in the past week. No history of withdrawal seizures or delirium tremens. He presents to clinic with the goal of abstinence.
- Current withdrawal symptoms: moderate anxiety

PATIENT CASE

- Other medical history:
 - Heart transplant (15 years ago, managed by transplant team)
 - Colectomy
 - Type 1 Diabetes (well-managed with insulin pump)
- Past treatments:
 - Has been given lorazepam for “panic attack”, which he thinks was a symptom of alcohol withdrawal at the time
 - Has tried gabapentin for nerve pain with success/tolerability
- Other Substance use: infrequent small amount of cannabis

PATIENT CASE

- Appropriate for ambulatory withdrawal over inpatient? **Yes**
- Current Severity of Withdrawal: **Mild withdrawal**
 - → Gabapentin 300mg TID, increase to 600 TID if tolerated
- Anxiety is a large withdrawal component of his past failure to cut down
 - Benzodiazepine was given as it may be more beneficial than gabapentin alone
 - → Lorazepam 1mg every 4 hours as needed (#6)
 - “Pt counseled on risks, determined to have good psychosocial stability, appears to be conservative with taking medications”
- Follow up:
 - RN phone check-in for days 1-3
 - Appointment with MD in 1-2 weeks

PATIENT CASE

- Day 1 phone check in: “doing great”, took one gabapentin 300mg dose
- Day 2 phone check in: having mild anxiety, increased to gabapentin 600mg QD
- Day 3 phone check in: gabapentin 600mg BID helping with anxiety and sleep
 - No lorazepam used

- Day 14 message: Requesting refill for lorazepam as it has been helpful for breakthrough anxiety
 - Continued abstinence from alcohol
 - He woke up from nightmare, had craving for alcohol, took lorazepam instead
 - Has been taking gabapentin 300/300/600mg, RN instructed him to try increasing to 600mg TID

PATIENT CASE

- Day 16 Follow up appointment:
 - Abstinent from alcohol, no cravings
 - Patient increased gabapentin to 600mg TID, no more anxiety episodes but feeling significant sedation which is bothersome
 - Asking for refill of lorazepam because it has been helpful
 - Provider clarified indications of lorazepam (for alcohol detox, not anxiety)
 - Discussed acute vs. protracted withdrawal
 - Reviewed increased risk of dependence to benzodiazepines in patients with AUD
 - Patient asked for small supply of lorazepam as he had a long flight coming up and thought it might help for flight anxiety

PATIENT CASE

- What would you do?

PATIENT CASE

- Assess for co-occurring psychiatric processes
 - Often have to wait and observe to diagnose
 - Treat as indicated
- Benzos for anxiety?
 - Not first line, not meant for monotherapy
 - Recommended for limited-time use, not meant to be a daily medication
 - Smaller, shorter supply limits risk of dependence
 - Choose longer-acting over shorter-acting options
 - Counsel patients thoroughly on risks
 - Set appropriate boundaries, ground rules **early on**
 - **Ultimately**: up to the individual prescriber and their relationship to the patient

PATIENT CASE

- Patient agreed to wait and see how his anxiety progressed with first line treatment
- Started escitalopram 10mg qdaily
- Reduced gabapentin down to 600mg qhs due to daytime sedation
- 9-week follow up: Denies anxiety and alcohol cravings, sleeping well
- Has not asked for benzos again

TAKE HOME POINTS

- Alcohol withdrawal is an uncomfortable and possibly life-threatening condition
 - Intervention improves safety and outcomes, and prevents “Kindling”
- Ambulatory withdrawal is appropriate for **mild to moderate (CIWA 15 or less)** withdrawal without other complicated conditions or history
 - Mild: Gabapentin (or carbamazepine)
 - Moderate:
 - Chlordiazepoxide or diazepam; lorazepam if liver concerns
 - Gabapentin
 - Adjunctive: supportive medications for specific symptoms of withdrawal

TAKE HOME POINTS

- After detox care:
 - Treatment program for alcohol use disorder
 - Gabapentin can be continued for treatment of AUD
 - If ongoing anxiety or other psychiatric symptoms, monitor and treat as indicated
 - Understand the risks of continuing benzodiazepine after detox is completed

BOTTOM LINE

- There is a small subset of patients for whom outpatient benzodiazepines are indicated for management of withdrawal
 - For prescribers who don't wish to use benzos, there are promising alternatives
 - For prescribers who do wish to use them, use them appropriately and with safeguards in place

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THANK YOU!