Maine Opioid Response Opioid Clinical Advisory Committee

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To: Maine hospital clinical and policy leadership, substance use treatment providers, and pharmacy communities

The Maine Opioid Response Clinical Advisory Committee consists of approximately 30 leaders in substance use disorder prevention, treatment and harm reduction in Maine including both prescribers and pharmacists. As part of our efforts, we have been working on developing clinical and policy recommendations related to the management of patients with substance use disorders (SUD), particularly as they encounter barriers within the existing health care delivery system.

One significant SUD treatment issue currently being faced in Maine is the lack of supervised withdrawal programs. Only three medically supervised withdrawal facilities in Maine accept MaineCare, and residential treatment facilities often have months-long waitlists, exacerbating the ongoing crisis for individuals with SUD who seek low barrier treatment options. To begin to address this issue, we offer both system-level and clinical-level recommendations for withdrawal management for opioids and alcohol, as well as accompanying policy recommendations. Our emphasis is on ensuring access for individuals seeking withdrawal management by providing resources and expertise in a variety of settings with easily navigable systems. This will enable individuals to receive a level of care appropriate both to their level of SUD severity, as well as their individual social circumstances and personal preferences. Our recommendations incorporate the recently updated ASAM Criteria, which emphasize low-barrier access and early integration of ongoing treatment (behavioral and pharmacologic) into withdrawal management episodes. We recognize that withdrawal management for opioids in the fentanyl era is a rapidly evolving field, presenting new challenges to buprenorphine induction, including delayed time to induction, a higher risk of precipitated withdrawal, and idiosyncratic reactions. Collaborative decisionmaking and informed consent with patients about withdrawal management options are crucial.

We are aware that many providers in the community have had limited experience with withdrawal management and that adoption of these guidelines will require ongoing clinical support and technical assistance, which will be offered through the Maine SUD Learning Community as well as other forums. These recommendations are intended to enhance care and should not replace a provider's own clinical judgement when providing withdrawal management care, and we encourage providers to seek expert opinion or a higher level of care if needed (and available). If you have any questions, please do not hesitate to contact us.

Sincerely,

Maine Opioid Response Clinical Advisory Committee

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Maine Opioid Response Clinical Advisory Committee: Proposed Position on Supervised Withdrawal Management

<u>Problem Definition</u>: Maine lacks systemic access to withdrawal management (WM) for alcohol and opioid use disorder in the sub-acute and outpatient settings. Barriers include the following:

- Lack of available beds/facilities (especially for MaineCare patients) in both the sub-acute and ambulatory setting, without adequate means to measure supply and demand
- Inadequate treatment protocols/guidelines to meet the needs of a changing substance use landscape
- High-barrier access procedures at existing withdrawal management centers
- Lack of adequate discharge and treatment planning (residential treatment, supportive housing, sober housing, outpatient treatment, etc.)
- Workforce development and retention (and reimbursement models to support them)

These topics are broad, and thorough recommendations on each require substantial analysis and documentation. This paper aims to provide high-level recommendations on two levels: system-level and clinical-level, with a specific focus on the ambulatory and sub-acute withdrawal management settings.

System-Level Recommendations

<u>1</u>. Expand access to withdrawal management services by developing comprehensive ambulatory and sub-acute withdrawal management services that meet ASAM Level of Care requirements, ensure highest possible quality of care, and adapt to practice environments in Maine.

ASAM provides a taxonomy of withdrawal management services at different levels of care, Level 1 through Level 4, updated in 2023.¹ These levels generally, but not necessarily, correspond to specific practice settings. For the purpose of *expanding access* to withdrawal management services in Maine, levels of care may be available in a variety of practice settings, provided they have sufficient staffing, resources and services available, as follows. [*Note that these are high-level recommendations, and more detailed State guidance on these requirements for WM services at each level of care is needed, drawing upon the most updated ASAM Criteria.*]

| Level of | ASAM Definition | Practice Setting(s) and Scope |
|-------------|---|--|
| Care | | |
| 1.7 | Ambulatory Withdrawal Management Without Extended On-Site Monitoring | -An organized outpatient service delivered by medical professionals who provide evaluation and management of intoxication, withdrawal, biomedical concerns, and common low complexity psychiatric concerns -May be delivered in primary care office setting, outpatient addiction program, Opioid Treatment Program (OTP), or mobile addiction treatment programs (e.g., street medicine) -Uniquely positioned to deliver low-threshold access² |
| 2.7 | Ambulatory Withdrawal Management With Extended On- Site Monitoring | -Can provide all care of Level 1.7 plus care for moderately severe intoxication and withdrawal with medical monitoring and nursing care during program hours, but not after-hours -May be delivered in primary care office setting (with appropriate resources for monitoring), addiction treatment or mental health care facility, day hospital setting, OTP |

| 3.7 | Medically Monitored Inpatient Withdrawal Management | -Provide medically managed residential services for patients who require 24-hour observation, monitoring and treatment but not the full resources of a hospital -May be delivered in stand-alone withdrawal management center, residential treatment setting or part of overlapping Level 4 center (specialty unit of acute care general or psychiatric hospital) |
|------|---|--|
| 4.0* | Medically Managed Intensive Inpatient Withdrawal Management | Organized services delivered by medical and nursing professionals that provide 24-hour medically directed care in acute care inpatient setting (general or psychiatric hospital) |

*Not in the scope of these recommendations

| Level | Staffing | Services, Supports and Resources |
|-------|---|--|
| of | | |
| Care | | |
| 1.7 | -Physicians, APP's and nurses with | -Ability to obtain comprehensive medical history and addiction- |
| | experience in addiction medicine | focused physical exam |
| | -Clinical staff (eg. counselors) | - Ability to initiate medication and management for low |
| | available directly or through | complexity psychiatric conditions |
| | formal affiliation | -Affiliation with higher levels of care for referral |
| | -Must have 24-hour access to | -Ability to do point of care and lab testing on-site |
| | general medical consultation | - Psychosocial and clinical services appropriate to level of care |
| 2.7 | -Physicians, APP's and nurses with | All Level 1.7, plus: |
| | addiction medicine experience | -Ability to provide hourly medical monitoring |
| | -Sufficient on-site staffing (eg. RN) | -Prescription services with essential medications on site |
| | for medical monitoring | -Provide at least 20 hours of clinical services per week |
| | -Must have 24 hour access to | comprised of medical care and psychosocial services to address |
| | addiction medicine physician/APP | addiction and co-occurring MH conditions |
| | -Clinical staff (eg. counselors) | - Established relationship with nearby Level 3.7 and 4 programs |
| | available directly or through | to support rapid transitions if needed |
| | formal affiliation | |
| 3.7 | -Staffed by physician/APP with | All Level 2.7, plus: |
| | addiction medicine certification | -24-hour observation, monitoring and treatment are available, |
| | available 24/7 by phone; to assess | but full resources of acute care hospital not necessary |
| | pt within 24 hours of admission; | -Inter-disciplinary team of clinicians available to assess and treat |
| | daily on-site monitoring and eval | the individual during WM stay and to arrange appropriate |
| | as needed | follow-up upon discharge, depending on range and severity of |
| | -24-hour onsite RNs to conduct | patient's problems |
| | nursing assessment on admission, | -Availability of injectable buprenorphine and naltrexone |
| | monitor pt and administer meds | |
| | on hourly basis | |
| | -RN supervisor available 24/7 | |
| | -Clinicians for treatment planning | |
| | and on-site treatment | |
| 4.0* | Physician sees patient daily, | Availability of all services required for acute medical withdrawal |
| | available 24/7 | management and intensive care as needed |
| | Nursing monitoring 24/7 | |

*Not in the scope of these recommendations

2. Improve access to withdrawal management through same-day and multi-modal access

In many states, the standard of care for WM is same-day access. WM centers should implement policies and procedures to ensure that patients who are at an "action" stage with regard to addressing their substance use disorder are able to be seen and treated same-day, especially for patients in moderatesevere alcohol withdrawal or at high risk for overdose. This may be enabled by having walk-in, phone, or online scheduling access for WM services.

3. Ensure facilities that provide withdrawal management monitor and report supply and demand

It is recommended that access to withdrawal management in the inpatient and outpatient settings be routinely monitored by treatment facilities. Standard of care for both opioid and alcohol withdrawal management is same-day access, particularly for patients requiring inpatient level of care for alcohol withdrawal management. Wait times for admission should be routinely monitored and provided on a voluntary basis by WM facilities, enabling the State and other funders to add beds, staffing, facilities as needed so that supply for outpatient and inpatient WM services meets demand.

4. Initiate addiction treatment services concurrent with withdrawal management services

Per updated ASAM Criteria (ibid), "when withdrawal management services are provided alone or separate from chronic disease management for addiction, only a minority of patients continue with ongoing addiction treatment, and recurrence and re-admission for withdrawal management are frequent with predictable consequences." Concurrent initiation of addiction treatment services (both behavioral and pharmacologic) should be an expectation of any WM service. In support of this goal, all medically managed programs for withdrawal should provide psychosocial services either directly or through formally affiliated providers or programs.

5. Integrate Discharge Planning and Coordination of Care into WM protocols and payment

It is well-documented that a withdrawal management episode (particularly for opioids) does not constitute treatment.³ In all WM settings, both treatment and discharge planning should begin the day of admission and be indexed to the patient's level of need (as determined by ASAM criteria) and preference for treatment setting. Discharge planning and coordination of care should be performed by trained SUD clinicians, with access to information and community resources to support patient treatment goals. In the case of an episode of WM for opioids, discharge with a prescription for MOUD and direct linkage to an MOUD provider is a minimum standard of care.

6. Ensure technical assistance, clinical supervision and compensation parity for WM Workforce

Given the increasing complexity of WM in all settings, and particularly for opioids, staff development and technical assistance is essential. It is recommended that all WM clinical staff (LMP's and nurses in particular) have access to expert technical assistance. This may come in the form of an ECHO, a webinar series, just-in-time consultation, or in-service presentations. Additionally, it is recommended that the State require one hour per month of documented group supervision and consultation to medical treatment staff, non-medical treatment staff, withdrawal management technicians, substance use disorder treatment staff, and any peer support or wellness specialist for Level 2.7 and above. The purpose of this supervision is to increase their skills within their scope of practice; improve quality of services or supports to patients; and ensure understanding and application of program policies and procedures.

Retention of trained, professional, and compassionate staff in WM settings is of paramount importance. These positions are equally important to any other clinical or staffing positions in the healthcare setting, inclusive of clinical and hospital settings. Compensation should be benchmarked to community standards, and WM centers must be reimbursed adequately to support fair compensation of their workers.

7. Create Quality Measures and Monitoring for Withdrawal Management Services

As with any healthcare service, withdrawal management services should be measured by, and strive for, specific quality measures that enhance the quadruple aim.⁴ Sample measures may include: linkage to care; ongoing engagement with SUD care; 30-day readmission rates; same-day access; or patient satisfaction surveys. Quality incentives should be built into payment models to support continuous improvement.

9. Adequate Reimbursement and Novel Reimbursement Models

None of the guidance in this document – whether in regard to clinical care, access, staffing, or quality – is possible without reimbursement levels and mechanisms that match the treatment settings and levels of care described herein. Additionally, reimbursement models must be nimble and adaptive to the ever-changing landscape of substance use disorder treatment. Changes in treatment regiments, treatment settings, workforce needs, and coordination of care can emerge rapidly, and reimbursement models must be flexible enough to accommodate these urgent needs.

Clinical Recommendations for Alcohol Withdrawal Management

Step 1. Assess Severity of Alcohol Withdrawal Syndrome (AWS) and Determine Level of care (LOC)

The severity of alcohol withdrawal syndrome must be diagnosed and determined in any patient with clinically significant alcohol consumption.⁵ LOC determination should be based on the least intensive level where the patient can be managed safely (see Appendix A for algorithm to assess level of care). Once the LOC has been identified and treatment is initiated, a patient should be closely observed to confirm the patient is in the correct LOC. The LOC may be reduced or increased as a patient's symptoms improve or worsen.

Several tools are available to assess and predict withdrawal management severity. The <u>CIWA-Ar</u> is most commonly used to assess severity, and provides an initial indication of level of care, with other factors considered.⁶ The Short Alcohol Withdrawal Scale (SAWS) can also be useful for patients to assess their own withdrawal during outpatient withdrawal management.⁷

While some patients with moderate withdrawal severity may be treated in the ambulatory setting, patients with moderate withdrawal severity with *any* of the following conditions should be referred for Level 3.7 or higher:

- Medical or psychiatric condition requiring inpatient treatment
- Physiologic dependence on benzodiazepines or Sedative Hypnotic Use disorder
- > 17 standard drinks/day
- Any history of DT's/seizure^{*}
- Social factors including unhoused and/or inappropriate housing situation (sole caregiver for children, etc.), lack of transportation to clinical practice

^{* *}This criterion will be re-visited in future guidance, as providers become more experienced with ambulatory WM

• Pregnancy, intolerance of oral medications, suspected head injury, inability to communicate symptoms, moderate or severe cognitive impairment, imminent risk of harm

Step 2. Provide Initial Evaluation and Treatment of Alcohol Withdrawal Syndrome

Urine drug screening should be obtained on all patients. If laboratory access is available, it is recommended to also obtain CBC, CMP, Hepatitis C antibody, and blood alcohol level. Routine physical examination (especially looking for stigmata of liver disease) should be performed.

Mild AWS. Mild withdrawal may be treated in the primary care setting or higher, with supportive care (education, low-stress home environment, fluids, multivitamin, thiamine supplementation), with or without pharmacotherapy. If medications are used, carbamazepine and gabapentin are reasonable options for monotherapy but do not reliably prevent withdrawal seizures or delirium tremens (see Appendix C for dosing).⁸ Gabapentin is effective in treating AUD; patients already taking it should continue during treatment of AWS.⁹

Moderate AWS. Moderate AWS may be treated in the outpatient treatment setting, or primary care setting, with the appropriate supports in place (see System Level Recommendations above). With regard to pharmacotherapy, benzodiazepines are a first-line therapy for patients experiencing moderate withdrawal symptoms, reducing the risk of seizure and the development of delirium tremens.¹⁰ Long-acting benzodiazepines (such as chlordiazepoxide or diazepam) are preferred, though a shorter-acting benzodiazepine may be selected for older patients or those with significant liver impairment.

Benzodiazepine dosing can be either fixed or symptom- triggered, and risks and benefits of benzodiazepine dosing regiments should be evaluated, as symptom-triggered may be more difficult in the ambulatory setting (see Appendix D for algorithm). Carbamazepine or gabapentin may also be used as adjuncts with benzodiazepine therapy, particularly if symptoms persist despite adequate benzodiazepine use. Gabapentin may reduce the need for benzodiazepines during withdrawal management.¹¹

Step 3. Perform daily follow-up for ambulatory alcohol withdrawal management

In the primary care and outpatient treatment settings, it is recommended to arrange daily follow-up for up to five days following evaluation and initiation of pharmacotherapy. Follow-up may take place inperson or by virtual (telephone or video) visit. Ideally, virtual visits will alternate with in-person visits. At follow-up, as available based on the visit modality, evaluate for:

- General condition, vitals, hydration, orientation, sleep and emotional status, substance use
- Blood alcohol concentration (if available at clinical location)
- Objective withdrawal scale assessment using CIWA-Ar if in-person or SAWS if virtual
- Clinical indications to stop ambulatory management and refer to a higher level of care:
 - Severe and un-resolving tremor despite multiple doses of medication
 - Persistent vomiting, hallucinations, confusion, seizure, agitation
 - Worsening underlying medical or psychiatric conditions
 - Over-sedation
 - Return to alcohol use
 - Syncope or unstable BP or HR

Step 4. Refer to/initiate higher level of care for Severe or Complicated AWS.

If a patient is not a candidate for outpatient withdrawal management (either initially or on follow-up), it is recommended that they be referred to sub-acute withdrawal management (Level 3.7) which can provide 24/7 medical staffing and support. Benzodiazepines are first-line treatment for alcohol withdrawal in the sub-acute setting, along with standing doses of gabapentin and additional adjunctive medications. Sample protocols are included in Appendix E.

Sub-acute withdrawal management centers are generally not able to provide care for individuals who are unable to perform their own activities of daily living, are unable to ambulate or transfer, are oxygendependent, etc. However, many hospitals will not admit people for the primary diagnosis of withdrawal management. It is recommended that Maine developed hospital-affiliated withdrawal management programs, which would allow for a higher risk population to obtain much needed WM treatment.

Clinical Recommendations for Opioid Withdrawal Management and Stabilization

Step 1: Determine Level of Care and Patient Preference for Withdrawal Management with Buprenorphine

Unlike withdrawal management for alcohol, level of care determination for opioid withdrawal management is less protocolized, and collaborative decision-making with patients regarding the best strategy and setting for withdrawal management with buprenorphine is essential.¹² One must consider and discuss social and emotional factors with patients, such as past experiences with withdrawal management, current life/living situation (unhoused is not necessarily an exclusion for outpatient withdrawal management), motivation, distress tolerance, and overall patient goals (comfort, speed, privacy).

Reasons to consider inpatient (level 3.7 or higher) withdrawal management include:

- Concurrent regular use of alcohol or benzos
- Other medical/psychiatric co-morbidities, particularly if unstable or triggered by stress
- H/o severe precipitated withdrawal/severe anxiety about process
- Unhoused and/or inappropriate housing situation (sole caregiver for children, etc.)
- Overall low distress tolerance
- High use pattern with daily IV fentanyl use

When 3.7 or higher withdrawal management is not available, or if a patient's social situation precludes an overnight stay, withdrawal management in a Level 2.7 setting is another possibility. This can be done in a single day, with observation for several hours, using high dose initiation or low-high dose initiation. In the latter case, it is optimal for the patient to self-administer low dose buprenorphine at home for 1-2 days, stop using opioids the day before admission, then come into office with medications for high-dose initiation and adjuncts.

Step 2: Determine Strategy for Opioid Withdrawal Management with Buprenorphine

The presence of fentanyl and fentanyl analogs in the US drug supply present new challenges to buprenorphine induction, including delayed time to induction, a higher risk of precipitated withdrawal with buprenorphine, and idiosyncratic reactions, including_intense dystonia and vomiting. Given this complexity, new strategies for withdrawal management (and specifically initiation onto buprenorphine)

have emerged. The following table provides sample initiation strategies, protocols, potential settings for each strategy, and advantages and disadvantages of each strategy:

| Strategy | Setting | Protocol | Pros | Cons |
|-------------------------------|---------------------|--------------------|-----------------------|-------------------------------|
| Standard Initiation | Level 1.7, 2.7, 3.7 | Start at 4-8mg, | Familiar | Less effective in fentanyl |
| | | titrate up to 32mg | Easier (no cutting of | era |
| | | | tabs/films) | Difficult to be in withdrawal |
| | | | | for long period of time, |
| | | | | patients may give up |
| Low-dose | Level 1.7,2.7 | Titrate up to 24mg | Less intimidating | Complicated |
| Initiation ¹³ | NOT 3.7 | +mg prn | than high dose | Takes a long time |
| | | | Lower chance of | Hard to stick to "quit date" |
| | | | precipitated w/d (in | |
| | | | theory) | |
| High Dose | Level 1.7, 2.7, 3.7 | Dose up to 32mg | Rapid | Can be intimidating to pts |
| Initiation ¹⁴ | | | Easier (one size tab | Hard to self-assess |
| | | | only, simple | readiness |
| | | | process) | Precipitated w/d can be |
| | | | | severe if occurs |
| Low-High Dose | Level 1.7, 2.7, 3.7 | Low dose for 24 | Rapid | Requires 2 different size |
| Initiation ¹⁵ | | hours, then high | Initial low dose | tabs |
| | | dose (up to 40mg) | decreases fear of | Requires tracking time and |
| | | (see citation) | high dose | # of doses |
| Naloxone to High | Level 1.7, 2.7 | Self-administer | VERY rapid (under | Requires high distress |
| Dose Initiation ¹⁶ | | naloxone, take 24 | an hour) | tolerance |
| | | mg, increase to | | |
| | | 32mg Day 2 | | |

Opioid Withdrawal Management & Buprenorphine Initiation Strategies

These protocols also provide additional insight into evolving requirements for buprenorphine initiation and maintenance. First, studies from the past several years have demonstrated that **buprenorphine doses up to 32mg are effective and may be required for stability**. Dosing at a maximum of 24mg buprenorphine is based on limited study of μ -receptor occupancy, which was not performed in the fentanyl era.¹⁷More recent studies have shown that buprenorphine increases μ -receptor occupancy in a dose-dependent fashion, with near-maximal effect at 32mg.^{18,19,20,21,22} A recent evidence review in the *Journal of Addiction Medicine* notes that "in light of established research and profound harms from fentanyl, the Food and Drug Administration's current recommendations on target dose and dose limit are outdated and causing harm. An update to the buprenorphine package label with recommended dosing up to 32 mg/d and elimination of the 16 mg/d target dose would improve treatment effectiveness and save lives."²³ Expanding access to the extended-release buprenorphine injectable may also be a good option.

Second, **use of buprenorphine monoproduct is the standard of care in many Level 3.7 withdrawal management facilities,** given that the adverse effect of sublingual naloxone is less benign and more prevalent than generally accepted, which can affect patient engagement in treatment. ^{24,25} Additionally, we cannot unambiguously conclude that naloxone is an effective deterrent to misuse of buprenorphine.²⁶ It is possible to utilize buprenorphine monoproduct for withdrawal management and stabilization, and then switch to the combination product. Given the controls in a Level 3.7 setting, buprenorphine monoproduct should be provided if a patient requests it. In the ambulatory setting, buprenorphine monoproduct should be selected for withdrawal management if there is a documented history of an adverse reaction to the combination product.

Step 3: Know and Use Specific and Scheduled Adjunctive Medications

Many of the symptoms of withdrawal from fentanyl are more severe and idiosyncratic than those from other opioids, and may require different adjunct medications, or adjunct medications at different strengths or formulations than previously used (see Appendix F for details). Additionally, scheduled adjuncts can be critical, eliminating the need to "chase symptoms." In the home setting, a support person to administer medications is ideal, but not required. Use of adjunct medications is particularly important for severe restlessness and anxiety associated with withdrawal from fentanyl, *even after maintenance dose is achieved*.

Policy Recommendations for Withdrawal Management

- To support the implementation of a continuum of care for withdrawal management services across the state, it is recommended that the State of Maine develop a comprehensive policy to establish requirements for withdrawal management services at all levels, based on the ASAM Level of Care criteria, to support individualized services that address geographic, cultural, and social appropriateness.
- 2. Given complexity of alcohol and opioid withdrawal management, adapt guidance and support for withdrawal management to provide same-day access for Level 3.7, as well as next day evaluation by LMP and opportunity for daily rounding by LMP if needed.
- 3. Ensure adequate funding streams to support comprehensive withdrawal management at all levels of care, as well as to support training and retention of staff, improved access and monitoring, quality measurement and incentives.
- 4. Provide support for Level 4/hospital-level withdrawal management as the primary diagnosis, for patients with severe AUD and OUD that do not meet criteria for Level 3.7 WD management or below.
- 5. Adapt MaineCare coverage to meet the evolving needs of buprenorphine initiation and maintenance in fentanyl era:
 - a. No PA requirement for buprenorphine monoproduct in withdrawal management setting
 - b. No PA requirement for buprenorphine dose <32 mg in withdrawal management setting
 - c. Collaborate with MaineCare DUR OUD workgroup to optimize access to buprenorphine in the outpatient setting.

Appendix A: Assessment of Withdrawal Severity and Level of Care Recommendation:



*This criterion will be re-visited in future guidance, as providers become more experienced with ambulatory WM

Appendix B: Sample Medication Regiments for Outpatient Alcohol Withdrawal Management

Gabapentin

Absolute contraindications: hypersensitivity to gabapentin Dose adjustments: reduce dose for renal impairment

Sample gabapentin dosing regimen²⁷

| Day | Gabapentin dosing |
|------------|---|
| Day 1 | 300 mg every 6 hours |
| Day 2 | 300 mg every 6 hours |
| Day 3 | 300 mg every 6 hours |
| Day 4 | 300 mg every 8 hours |
| Day 5 | 300 mg every 12 hours |
| Day 4 6 | 300 mg for one dose, then stop |
| Sample sig | Gabapentin 300 mg capsules, take one capsule every 6 to 24 hours, #18 capsules, zero refills |

For maintenance therapy, gabapentin 600mg TID has been shown to have dose-dependent benefits for abstinence, relapse to heavy drinking and cravings post-withdrawal management.²⁸

Carbamazepine

Absolute contraindications: Concomitant MAOI, nefazodone, delavirdine use. History of bone marrow depression, history of hypersensitivity to a tricyclic antidepressant (e.g. amitriptyline), known hypersensitivity to carbamazepine

Dose adjustments: avoid in patients with significant liver dysfunction, consider gabapentin (see above) Additional considerations: Avoid in patients with significant liver disease, patients of Asian and South Asian ancestry should be considered for HLA-B*1502 allele testing prior to being prescribed carbamazepine; If duration of therapy exceeds 5 – 7 days, carbamazepine's induction of CYP450 3A4 becomes important and clinically significant drug interactions with antidepressants, antipsychotics, opioids, and others may occur, typically resulting in lower levels of the substrate and clinical failure.

Sample carbamazepine dosing regimen²⁹

| Day | Carbamazepine Dosing |
|------------|---|
| Day 1 | 400 mg twice daily |
| Day 2 | 400 mg twice daily |
| Day 3 | 200 mg qam, 400 mg qhs |
| Day 4 | 200 mg qam, 400 mg qhs |
| Day 5 | 200 mg twice daily, then stop |
| Sampla sig | Carbamazepine 200 mg generic tablets, take one to two tablets |
| Sample sig | twice daily, #12 tablets, zero refills |

Chlordiazepoxide

Absolute contraindications: known hypersensitivity to chlordiazepoxide Dose adjustments: avoid in patients with significant liver dysfunction and consider oxazepam instead (see below)

Fixed dose scheduled chlordiazepoxide taper templates:

<u>NOTE: in addition to the medication it is recommended to provide a</u> few additional take-home doses for breakthrough symptoms. In the sample sig's below, 4 additional 25 mg chlordiazepoxide doses are included.

| | Chlordiazepoxide dose (daily alcohol consumption < 9 US standard drinks) | Chlordiazepoxide dose (daily alcohol consumption between 9 and 17 US standard drinks) | Daily alcohol consumption > 17 US standard drinks |
|---------------|---|---|---|
| Day 1 | 25 mg four times a day | 50 mg four times a day | |
| Day 2 | 25 mg three times a day | 50 mg three times a day | |
| Day 3 | 25 mg twice a day | 25 mg four times a day | Investigat |
| Day 4 | 25 mg at night | 25 mg three times a day | withdrawal |
| Day 5 | | 25 mg two times a day | management |
| Day 6 | | 25 mg at night | recommended |
| Sample sig | Chlordiazepoxide 25 mg capsules, take one capsule one to four times daily, #14 capsules, zero refills | Chlordiazepoxide 25 mg capsules, take one to two capsules one to four times daily, #28 capsules, zero refills | |

Hold scheduled dose for increased sedation. Monitor SAWS score as needed for increased withdrawal symptoms, for SAWS score >18 that is unresponsive to available medications, contact provider or present to ER

| | Chlordiazepoxide dose* (daily alcohol consumption < 9 US standard drinks) | Chlordiazepoxide dose* (daily alcohol consumption between 9 and 17 US standard drinks) | Daily alcohol consumption > 17 US standard drinks |
|---------------|---|--|---|
| Day 1 | 25 mg every four hours* | 50 mg every four hours* | |
| Day 2 | 25 mg every six hours* | 50 mg every six hours* | Innatient |
| Day 3 | 25 mg every six hours* | 25-50 mg every six hours* | withdrawal |
| Day 4 | 25 mg at night* | 25-50 mg every 12 hours* | management recommended |
| Day 5 | | 25 mg every 12 hours* | |
| Day 6 | | 25 mg at night* | |
| Sample sig | Chlordiazepoxide 25 mg capsules, take one capsule one to six times daily, #15 capsules, zero refills | Chlordiazepoxide 25 mg capsules, take one to two capsules one to six times daily, #35 capsules, zero refills (consider offering this in portions over multiple visits within the 5 day period | |

*For Short Alcohol Withdrawal Scale (SAWS) score ≥ 12

Monitor SAWS score as needed for increased withdrawal symptoms, for SAWS score >18 that is unresponsive to available medications, contact provider or present to ER

Oxazepam:

Absolute contraindications: known hypersensitivity to oxazepam In patients with significant liver dysfunction, consider substituting oxazepam for chlordiazepoxide in the above dosing regimens. 20 mg of oxazepam is equivalent to 25 mg of chlordiazepoxide.

Diazepam:

Absolute contraindications: known hypersensitivity to diazepam. If chlordiazepoxide not available, or if concern for over-sedation, consider substituting diazepam for chlordiazepoxide in the above dosing regimens. 5-10 mg of oxazepam is equivalent to 25 mg of chlordiazepoxide.

Appendix C: Considerations for Fixed vs Symptom-triggered Benzodiazepine Taper for Ambulatory Alcohol Withdrawal Management



| □Consent to chart | o receive benzodiazepine m | edications sigr | ned and in | Symptom-triggered BZD adjunct orders |
|----------------------|-----------------------------|----------------------------------|--------------------------------|---|
| Assess patier | nt Q4-6 hours until CIWA-A | r ≥ 10, then: | | for alcohol WM: |
| If CIWA-Ar | □ Give Diazepam (Valium) | □ Give Oxazepam (Serax) | And redo CIWA- Ar within | Default additions for alcohol WM: unless crossed out, initiate: - Thiamine 100 mg PO daily for three total doses |
| > 25 | 40 mg po | 75 mg po | 1 hour | stop early at patient's request |
| 20 – 25 | 30 mg po | 60 mg po | 2 hours | |
| 15 – 19 | 20 mg po | 40 mg po | 4 hours | Default adjunct for alcohol WM: |
| 10 - 14 | 10 mg po | 20 mg po | 6 hours | Gabapentin 600 mg PO BID x3 days, then |
| < 10 | None | None | 6 hours | soo mg ro bio xs days, then stop |

Appendix E: US Standard Drink Conversion Table

| Alcohol category | Also known as | Volume | % ABV* | # drinks | | |
|--|-----------------------------|--------|-----------|-------------|--|--|
| Beer | Bottle, can | 12 oz | 5% | 1 | | |
| | Tallboy | 16 oz | 5% | 1.5 | | |
| | Tallboy, bomber | 22 oz | 5% | 2 | | |
| | Forty | 40 oz | 5% | 3.3 | | |
| Malt liquor | Tallboy | 16 oz | 6-8% | 2-3 | | |
| | Tallboy | 16 oz | 12% | 4 | | |
| | Tallboy, 4 Loko | 24 oz | 12% | 5 | | |
| | Forty | 40 oz | 12% | 8 | | |
| Wine | Glass | 5 oz | 12% | 1 | | |
| | Bottle | 26 oz | 12% | 6 | | |
| | Magnum | 1.5 L | 12% | 12 | | |
| | Jug/cask/box | 3-5 L | 12% | 24-40 | | |
| Alcohol | Shot | 1.5 oz | 40% | 1 | | |
| | Nip | 2 oz | 40% | 1.6 | | |
| | Pint | 16 oz | 40% | 11 | | |
| | Fifth | 26 oz | 40% | 17 | | |
| | Liter/Quart | 32 oz | 40% | 21 | | |
| | Handle, 1/2 gallon | 1.75 L | 40% | 40 | | |
| *Standard ABVs listed, if patient reports drinking a different | | | | | | |
| %ABV product (e.g 100 proof (50% alc/vol) liquor), adjust | | | | | | |
| stanuara arir | standard drinks accordingly | | | | | |

Adapted from: https://www.integration.samhsa.gov/clinical-practice/sbirt/Stnd-Drink-Ruler- chart.pdf

Appendix F: Sample Adjunctive Medications for Fentanyl Withdrawal Management

| Symptom | Medications and Dosing | Notes | | |
|-------------------------|--|---|--|--|
| Muscle Spasms/ | Tizanidine 2mg QID | | | |
| Dystonia | Methocarbamol 1000mg QID | | | |
| Nausea | Ondansetron starting dose at 8mg (4mg less effective with fentanyl) Judicious use of promethazine; monitor for over-sedation | Nausea can be particularly severe in patients with IV fentanyl use | | |
| Anxiety | Clonidine up to 0.3mg QID Diphenhydramine | Anecdotally, diphenhydramine tends to work better than hydroxyzine in fentanyl withdrawal | | |
| Restlessness/agitation: | Gabapentin up to 900mg TID Olanzapine 5mg BID or TID | Use high doses of gabapentin in first 3 days, then taper or stop | | |
| Pain | Ibuprofen 800mg QID APAP 1000mg QID | Higher doses for only a short period of time; consider contra- indications (NSAIDs: cardiovascular disease, renal failure, gastric ulcer; Acetaminophen: active AUD and liver disease) | | |
| Sleep | Trazodone 100mg qhs Quetiapine 50-100mg Mirtazapine 15mg | Try quetiapine or mirtazapine if trazodone ineffective | | |

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