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Health Update

Emerging practices for managing medetomidine withdrawal in the outpatient setting
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Morbidity and mortality from drug use in Philadelphia remain a public health priority. Although overdose deaths decreased in 2024, the addition of medetomidine to the drug supply has led to severe health consequences.[1] Since medetomidine was first detected in Philadelphia in April 2024, emergency room visits for withdrawal have increased by 291%. There is increasing recognition that alpha-2-agonist dependence and withdrawal from medetomidine require dedicated treatment. Over the past two years, healthcare systems have updated hospital protocols to treat medetomidine withdrawal.[2–4] However, there has been less focus on the management of medetomidine withdrawal in the outpatient setting. To address this gap, on May 5, 2026, the Substance Use Response, Guidance, and Education Program at the Health Federation of Philadelphia hosted a webinar on outpatient management of medetomidine withdrawal, "From REbound to REcovery: Managing the Alpha-2 Agonist Storm in Outpatient Settings," provided by experts in primary care, street medicine, opioid treatment programs, and lived experience. This Health Update provides a summary of that training, which can also be accessed here: https://surge.learn.healthfederation.org/plus/

SUMMARY POINTS

- Patients being discharged from the hospital after receiving treatment for medetomidine withdrawal to the outpatient setting should see a provider for follow-up ideally within 2-5 days for monitoring of vital signs and medication adjustment.
- Clonidine dose at hospital discharge for a patient discharged to the community should not exceed 0.3mg three times a day.
- Tapering of clonidine post-hospitalization for medetomidine withdrawal can take up to several months. At least weekly clinic visits are suggested initially.
- Providers should assess for current drug use to inform clonidine tapering, treatment efficacy, and educate patients on symptoms of low blood pressure.
- Clinical factors to consider for referral to inpatient hospital admission include very elevated blood pressure, inability to tolerate medications by mouth, history of previous treatment for medetomidine withdrawal in the hospital, and underlying co-morbidities.

Disclaimer: the published literature on medetomidine withdrawal is limited to retrospective cohort studies, case studies, and expert opinion in the inpatient setting. This is still an emerging clinical presentation. Best practices are based on the experience of outpatient clinicians caring for people who use drugs in Philadelphia.

Post-hospitalization discharge planning and clonidine tapering

Due to the severity of medetomidine withdrawal, the acute care hospital setting is increasingly where people who use drugs are receiving withdrawal treatment and being inducted on methadone or buprenorphine for their opioid use disorder. At hospital discharge, many patients still require high doses of alpha-2-agonist therapy that require tapering over several months. Clonidine is the most effective alpha-2-agonist therapy for treating medetomidine withdrawal in the outpatient setting. High doses of clonidine are often used during inpatient admissions, but this should be tapered during the hospitalization so that patients can be discharged on a safe outpatient dose of clonidine. A clonidine regimen of 0.3mg three times a day is the maximum dose and frequency for outpatient withdrawal management and should be a goal for hospital discharge with outpatient follow-up.

After hospital treatment for medetomidine withdrawal, patients need close follow-up for blood pressure monitoring and medication management. A goal should be for patients to see an outpatient provider within at least 2-5 days of hospital discharge. Close post-hospitalization follow-up can be facilitated by working with peer navigators, who can communicate directly with the patient and their follow-up outpatient provider. After post-hospitalization linkage to

outpatient care is established, regular weekly visits are necessary to ensure safe and effective tapering of clonidine. Initially, and at higher clonidine doses, clinicians should prescribe clonidine in 1-week increments to ensure the dose is safely titrated to blood pressure. (see Table 1)

Table 1: Blood Pressure Parameters for Titrating/Tapering Clonidine Dose for Outpatient Medetomidine Withdrawal Treatment

Patient Office Presentation	Blood Pressure Range	Clonidine Titration/Taper
Low Blood Pressure	80-110/50-70	Reduce clonidine dose by at least 1/2 to 2/3
Normal Blood Pressure	110-140/70-90	Keep at the same dose, and plan for a slow decrease over time (e.g., reduce 0.1mg in 1-2 weeks)
Elevated Blood Pressure	140-180/90-110	Increase the dose of clonidine or increase frequency, consider adding guanfacine or tizanidine
Very Elevated Blood Pressure	>180/110	Consider hospitalization

The use of clonidine patches should be tailored to each patient. Clonidine patches offer the advantage of medication delivery without requiring adherence to an oral regimen. However, patients will not be able to rapidly change their clonidine dose in response to changes in substance use or symptoms of high or low blood pressure. In addition, having a clonidine patch in place may worsen low blood pressure due to non-withdrawal factors such as infection, dehydration, or return to use. Patches should always be dated, including the time of application and dose.

Blood pressure management and counseling

Clonidine is an anti-hypertensive medication, so it is important to monitor blood pressure weekly initially and titrate the clonidine dose as described in Table 1 above. Integrating blood pressure management and counseling has not historically been part of opioid withdrawal management and may require changing clinic workflows. There are several considerations outpatient clinicians can keep in mind when monitoring blood pressure and using alpha-2-agonists to manage medetomidine withdrawal that are described in Table 2 below.

Table 2: Clinical Considerations for Alpha-2-agonist Selection in the Outpatient Setting

Clinical Situation	Alpha-2-agonist Selection
Blood pressure/heart rate stable or elevated	Clonidine and Tizanidine
Blood pressure/heart rate low	Tizanidine and Guanfacine
EKG indicating prolonged QTc interval	Guanfacine or Clonidine
Withdrawal symptoms not adequately controlled with current alpha-2-agonist therapy	Addition of other agents as needed if clonidine has been maximized to the highest safe outpatient dose, consider inpatient admission for dexmedetomidine if the patient cannot tolerate medications by mouth

Importantly, it is not uncommon for patients to continue to use drugs while their medetomidine withdrawal symptoms are being managed in the outpatient setting. Using fentanyl with medetomidine can lead to marked fluctuations in blood pressure. (note: “tranq dope” and “tranq” are terms used in reference to illicit fentanyl with medetomidine) Thus, outpatient providers managing medetomidine withdrawal should regularly have open and non-judgmental conversations with their patients about their current drug use. Information about patients’ current drug use can inform clonidine tapering and counseling on blood pressure. Example questions about drug use include:

- Are you using tranq dope or tranq?
- How often do you use tranq dope or tranq?
- How much do you use tranq dope or tranq?
    - The amount of drug use is often described in the number of bags or bundles per day. If a patient describes using a bundle, then clinicians may ask how many bags are typically in a bundle.
- Is that more or less than you used before starting treatment of tranq withdrawal?

Clinicians should monitor the amount and frequency of use to help determine treatment efficacy. When patients continue to use drugs, a reduction in use is an indication of effective withdrawal treatment. As patients gradually reduce drug use and plan for complete cessation, alpha-agonist medications will need to be increased, and additional

medications should be considered to treat symptoms of withdrawal. If a patient is using tranq dope/tranq while also receiving outpatient care for medetomidine withdrawal, then clinicians should consider the following counseling:

- Recommend not taking clonidine if planning to use or have recently used tranq dope/tranq.
- Provide education on symptoms of low blood pressure: lightheadedness or dizziness, fainting (i.e., syncope), changes in vision (e.g., tunnel vision, blurred vision), and increased confusion.
- Provide anticipatory guidance if a patient is experiencing symptoms of low blood pressure, such as:
    - Not taking the next dose of clonidine
    - Sitting or lying down to avoid injury
    - Increasing intake of salt (e.g., salty snacks) and hydration
    - Attempt maneuvers to increase blood pressure, such as squatting or sitting with legs crossed[5]

Emerging strategies for outpatient management of co-occurring opioid and alpha-2-agonist withdrawal
To date, medetomidine in the drug supply is nearly always detected with fentanyl. In Q1 2026, medetomidine was detected in 90% of drug samples where fentanyl was the primary drug in Philadelphia.[6] Thus, successful management of medetomidine withdrawal requires management of opioid withdrawal. There are two emerging strategies for outpatient management of both medetomidine and opioid withdrawal:

- The co-management approach has been described in the opioid treatment program setting, where the induction onto methadone is gradual over several days, but this approach may also be applied to outpatient buprenorphine micro-inductions. The co-management approach relies on patients reducing use of illicit substances as the dose of methadone or buprenorphine increases, which can lead to a "self-taper" from medetomidine that can be supported by prescribing alpha-2-agonists as needed.

- The sequential approach focuses on rapid induction onto buprenorphine, such as direct-to-inject administration of long-acting injectable buprenorphine for stabilization of opioid use disorder during active drug use (e.g., Brixadi™, Sublocade™) followed by dedicated management of alpha-2-agonist withdrawal with clonidine and additional alpha-2-agonists as needed to help reduce drug use. In this approach, patients should not change their use patterns significantly until they are fully stabilized on buprenorphine. Changing use patterns before being fully stabilized on buprenorphine will bring on symptoms of medetomidine withdrawal, which can create confusion given overlapping symptoms of opioid and alpha-2 agonist withdrawal.

In addition to clonidine, the following medications may be used to treat medetomidine withdrawal in the outpatient setting:

- Alternative/Adunct Alpha-2-agonists to consider in the setting of normal or low blood pressure but ongoing symptoms of withdrawal or cravings:
    - Guanfacine: 0.5–1 mg PO nightly or BID; titrate every 3–7 days; less hypotension/sedation
    - Tizanidine: 2–4 mg PO every 6–8h PRN; helpful when BP is lower but patients are still experiencing symptoms of medetomidine withdrawal; monitor for sedation and liver function tests
- Symptom-targeted adjuvants (short-term):
    - Nausea/vomiting: promethazine 12.5–25 mg PO q6h PRN; prochlorperazine 5–10 mg PO q6h PRN
    - Severe nausea/agitation: olanzapine 2.5–5 mg PO nightly or BID
    - Anxiety: hydroxyzine 25–50 mg PO q6h PRN
        - Avoid routine benzodiazepines; reserve short courses for select patients with close follow-up
    - Sleep/anxiety: gabapentin 300–600 mg PO TID (adjust to renal function)
    - Sleep/appetite: mirtazapine 7.5–15 mg PO nightly

Some of these medications can prolong the patient's QT interval. Depending on the patient's risk (treatment with methadone, underlying cardiac comorbidities, propensity for electrolyte abnormalities, etc.), providers can monitor EKGs to ensure the QT interval is safe.

Clinical factors to consider for inpatient treatment
Patients who are being managed for medetomidine withdrawal in the outpatient setting may need to be referred for inpatient hospitalization. For example, if their blood pressure is very elevated or they cannot tolerate medications by

mouth because of severe nausea and vomiting (see Table 1 and Table 2). Additional clinical factors that can help inform when patients may need inpatient treatment include:

- History of requiring admission to the hospital for medetomidine withdrawal in the past, which may be an indicator that they are more likely to experience severe symptoms requiring intensive care again when they stop using drugs.
- History of other co-morbidities, such as heart disease, strokes, and seizure disorders, which can increase the risk of complications from hypertensive urgency and nausea and vomiting associated with medetomidine withdrawal.

Resources
Medetomidine resources and treatment recommendations: www.substanceusephilly.com/medetomidine

Substance Use Disorder Treatment:
- Behavioral Health Services Initiative (uninsured): 1-215-546-1200
- Community Behavioral Health (Medicaid): 1-888-545-2600
- CareConnect Warmline: 484-278-1679
- DBHIDS Medication Assisted Treatment: https://dbhids.org/services/addiction-services/mat/
- SAMHSA National Helpline: 800-662-HELP (4357)

Recommend patients try not to use alone. If that is what they are doing, then advise them to call the Never Use Alone hotline: 877-696-1996

Learn how to get and use naloxone: www.substanceusephilly.com/get-supplies

Get naloxone and fentanyl test strips shipped to you for free and confidentially: nextdistro.org/philly

Learn how to use fentanyl test strips:
- https://www.substanceusephilly.com/trainings#trainingvideos
- www.cdc.gov/stopoverdose/fentanyl/fentanyl-test-strips.html
- www.youtube.com/watch?v=GmhE6UOZ9YY

Take a wound care training: www.substanceusephilly.com/trainings#xylazinetraining

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