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To: Hospitals and Clinics; BSAS Licensed and Approved Providers

From: Jessica Zeidman, MD, Deputy Commissioner, Chief Medical Officer and Alexander Y. Walley, MD, MSc, Medical Director, Bureau of Substance Addiction Services (BSAS)

Re: Medetomidine in the Massachusetts Opioid Supply and Medetomidine Withdrawal

Date: October 21, 2026

Dear Providers,

The purpose of this Clinical Advisory is to provide an update on the presence of medetomidine in the unregulated opioid supply in Massachusetts, to educate providers on clinical considerations related to medetomidine withdrawal, and to share additional resources on the topic. There have been increasing reports of medetomidine in the unregulated opioid supply across the United States and clinical cases of severe withdrawal due to medetomidine exposure among people who use drugs in several US cities. In Massachusetts, there have been several confirmed cases and additional suspected cases of medetomidine withdrawal in emergency department and hospitalized patients.

What is medetomidine?

- Medetomidine is a sedative being mixed with the unregulated opioid supply.
- Medetomidine is an alpha-2 agonist, like clonidine, dexmedetomidine, and the veterinary sedative xylazine. Xylazine has also been mixed with the unregulated opioid supply.[1] Medetomidine is more sedating and longer lasting than xylazine. A clinical alert for xylazine was released in 2023.

[1] https://www.mass.gov/doc/clinical-advisory-on-presence-of-xylazine-in-the-massachusetts-drug-supply-april-12-2023/download

Medetomidine in the Massachusetts opioid supply and clinical cases of medetomidine withdrawal

- Medetomidine was first identified in the unregulated opioid supply in Massachusetts in June 2024, and it has since been identified in samples from every county in the state, most commonly in the Central and Western regions.
- For the most recent community drug checking data, visit the Massachusetts Drug Supply Data Stream (MADDS).
- In the Spring of 2026, multiple hospitalized patients were diagnosed and treated for medetomidine withdrawal in Massachusetts hospitals in the Boston and Springfield/Holyoke regions.

What is concerning about medetomidine?

Medetomidine in the unregulated opioid supply contributes to overdose via profound and prolonged sedation. Effects of medetomidine intoxication and overdose include:

- Marked and prolonged sedation *that does not respond to naloxone*
- Bradycardia and hypotension
- Respiratory depression *that does respond to naloxone*

People who use drugs mixed with medetomidine can become physically dependent. After their last drug use, they might have withdrawal symptoms specific to medetomidine in addition to withdrawal from other substances. The transition from sedative intoxication to activated withdrawal can be abrupt and variable, with rapid progression within hours of last use. Signs and symptoms of medetomidine withdrawal that distinguish it from opioid withdrawal include:

- Severe vomiting and nausea (intractable in some cases)
- Tremor and myoclonic jerks
- Marked autonomic dysfunction, including tachycardia and marked hypertension (systolic blood pressure often > 180mmHg)
- Anxiety or agitation with reduced or intermittent responsiveness
- Diaphoresis
- Minimal response to typical opioid withdrawal or nausea medications

As a hyperadrenergic state, medetomidine withdrawal can potentially lead **to hypertensive crisis, cardiac arrhythmias, heart attack, stroke, and rhabdomyolysis.**

What should I do if I suspect medetomidine withdrawal?

The recommendations below are intended to provide guidance to providers treating medetomidine withdrawal; each patient should be evaluated and treated individually based

on their clinical presentation and unique needs. People who present in severe withdrawal may have co-occurring critical diagnoses that may be missed by attributing all symptoms to withdrawal. Clinicians should keep a high index of suspicion for other diagnoses, such as infection and exacerbation of co-morbid chronic illness.

- Initial treatment:
    - Early initiation of alpha-2-agonist therapy with maximum tolerated doses of clonidine.
        - Initiate oral clonidine 0.2 mg x 2-3 oral doses every 2 hours with hold parameters for hypotension, bradycardia, and sedation. While clonidine patches are also helpful, their onset of action is delayed and may not take effect for 12-24 hours.
        - Oral tizanidine or guanfacine can be used as an alternative to clonidine.
        - Escalate to dexmedetomidine 1 mcg/kg IV bolus, then infusion titrated 0.5- 1.5 mcg/kg/hr for persistent nausea and vomiting that makes oral alpha-2 agonist dosing not possible and persistent severe hypertension (SBP>180).
    - Treat vomiting, as vomiting restricts the use of oral medications and is an indication for intubation if severe and unable to protect airway.
        - Olanzapine 10mg IV/PO, prochlorperazine 10mg IV, or droperidol 2.5- 5 mg IV/IM have performed better than ondansetron or benzodiazepines.
        - Monitor for EKG and laboratory abnormalities including arrhythmias, prolonged QT interval, hypokalemia, hypomagnesemia, troponin, and lactic acid.
    - Some patients may require intubation for airway protection in the setting of vomiting or sedation.
    - Manage opioid withdrawal, as medetomidine is in fentanyl drug samples that are sold as opioids. Using clinical judgment regarding mental status and respiratory status, administer an initial oral methadone dose of 30 to 50mg and then 10mg additional every 4-6 hours (for a maximum initial dose of 60 mg in the first 24 hours) and oral hydromorphone 4-8 mg every 3-4 hours for breakthrough withdrawal or pain.
        - For patients who cannot take oral medications, administer an initial IV or IM methadone dose of 10- 25 mg as a starting dose and 5mg additional every 4-6 hours, and IV or IM hydromorphone 1-2 mg every 3-4 hours for breakthrough withdrawal or pain.
        - In cases where methadone is contraindicated (e.g., QTc prolongation or prior methadone exposure), administer IV or IM hydromorphone 1- 2 mg

every hour until opioid withdrawal symptoms are improved, holding for sedation.
    - Screen and maintain a high index of suspicion for concurrent alcohol and benzodiazepine withdrawal.
- Subsequent treatment
    - If required, dexmedetomidine infusions can typically be weaned with overlapping oral alpha-2 agonists over 24-72 hours.
    - Oral alpha-2 agonists can typically be weaned after 3-5 days.
    - When checking urine toxicology, send for medetomidine-specific testing to confirm diagnosis. Lab results can be difficult to interpret at some labs, so confirm the presence or absence of medetomidine by speaking with the send-out lab clinician. Send-out medetomidine-specific tests may take 7 days for results.

For those in community settings: What to look out for and know

- If your patients or clients have used drugs recently and experience these symptoms, encourage them to get medical help right away.
- Medetomidine is often found with fentanyl, so giving naloxone (Narcan) for respiratory depression from overdose is still recommended and effective to restore breathing. During an overdose, the goal of naloxone administration is the restoration of normal breathing, not wakefulness. Medetomidine may keep a person sedated even after successful opioid reversal.

Keep watching the affected person and always call 911 if you can.

- Test strips that detect medetomidine are available. StreetCheck maintains a map of community drug checking services at locations around New England.

Additional resources:

- **Medetomidine: Rising Adulterant in the Illicit Drug Supply**
  This fact sheet equips providers with essential information to recognize and treat medetomidine withdrawal syndrome. This fact sheet equips providers with essential information to recognize and treat medetomidine withdrawal syndrome. Developed February 2026.
- **Medetomidine**
  This resource page offers clinical guidance on recognizing medetomidine overdose and withdrawal and managing medetomidine withdrawal. Developed April 2025.
- **Emergence of Medetomidine in the Illicit Drug Supply: Implications for Emergency Care and Withdrawal Management**

This literature review discusses the emergence of medetomidine as an adulterant in the drug supply and reviews pharmacology, toxicity, and withdrawal management. Published online January 2026.

- **Medetomidine Withdrawal Treatment Guideline**
  This guideline outlines the clinical treatment pathway for medetomidine withdrawal. Developed September 2025.
- **Medetomidine Infiltrates the US Illicit Opioid Market**
  This viewpoint article discusses the introduction of medetomidine into the US opioid market and highlights the need for monitoring and a public health response. Published online September 2024.
- **Health Update: Responding to overdose and withdrawal involving medetomidine**
  This public health update from Philadelphia provides clinical guidance on responding to opioid overdoses involving medetomidine and managing medetomidine withdrawal syndrome. Developed June 2025.
- **Understanding Medetomidine: Emerging Challenges for Addiction Medicine**
  This episode of the ASAM Practice Pearls podcast discusses the regional spread of medetomidine in the drug supply, clinical approaches to managing withdrawal, and preparing a public health response. Episode from February 2026.
- **2026 Adapted Medetomidine Withdrawal Resource** (English/Spanish available)
  This handout provides a quick explainer for people who may have been exposed to medetomidine.
- **Medetomidine Drug Supply Alert**
  This fact sheet for first responders provides an overview of responding to withdrawal and overdose and a few community safety resources.
- **SafeSpot Hotline:** peer-run, anonymous hotline you can call 24/7 and someone will stay on to spot you when using alone. Call 800-972-0590 or visit the SafeSpot website.
- Get free naloxone from YouCan.
- Learn about drug checking services from StreetCheck or connect with a local harm reduction program.