IMAPP

Medetomidine Withdrawal

Medetomidine Objective Withdrawal Scale (MOWS)

Pouya Azar, Jessica Machado, Jane Kim, James Wong, Sahithi Thotakura, Jacky Siu, Anthony Lau, Sarah Haddleton, Keegan Epp, Nick Matthew & Victor Li.

This pilot withdrawal management protocol has not been evaluated yet through clinical trials and will need validation to assess safety and efficacy.

Executive Summary

Medetomidine has emerged as a novel adulterant in the illicit fentanyl supply and is increasingly associated with severe toxicity and withdrawal syndromes that differ meaningfully from opioid and benzodiazepine withdrawal alone. Reports from multiple jurisdictions describe rapid clinical deterioration driven by autonomic hyperactivity, with some cases requiring intensive care–level support.

In response to these emerging patterns, IMAPP has developed the Medetomidine Objective Withdrawal Scale (MOWS), a structured clinical protocol to support early recognition, monitoring, and management of suspected medetomidine withdrawal. This document provides epidemiologic context, pharmacologic rationale, and a standardized treatment protocol intended to support clinicians and health systems responding to this evolving toxidrome.

Key Points at a Glance

- Medetomidine is a potent α-2 adrenergic receptor agonist increasingly detected as an adulterant in illicit fentanyl.
- Withdrawal may present with marked autonomic hyperactivity and can persist despite appropriate treatment of opioid and/or benzodiazepine withdrawal.
- In British Columbia, medetomidine has been detected in over 30% of unregulated opioid samples as of December 2025.[13]
- In Philadelphia, complications related to medetomidine exposure have been reported to account for approximately 25% of ICU bed occupancy during peak periods.[21]
- IMAPP has developed the MOWS protocol to support structured recognition, scoring, and management using clonidine, with clear escalation criteria.

Contents

Key Clinical Features of Medetomidine Withdrawal

Symptoms of medetomidine withdrawal may begin within 4-6 hours of last use and can fluctuate over several days.

Common findings

- Tachycardia
- Hypertension
- Whole-body shivers (distinct from benzo/EtOH tremor)
- Diaphoresis
- Agitation or delirium (including hallucinations)
- Nausea or vomiting [2]

Background

- Medetomidine ("rhino tranq" or "mede") is a potent α-2 adrenergic receptor agonist originally used in veterinary anesthesia.[1]
- It has emerged as a novel adulterant in the illicit fentanyl supply across North America.[1]
- Compared with xylazine, medetomidine exhibits substantially greater α-2 receptor potency, with more pronounced and longer-lasting sedative effects and poor responsiveness to protocols previously developed for xylazine.[4,5]

Epidemiology

- Detections of medetomidine have occurred sporadically across North America since 2022, with spread documented across at least 18 U.S. states.[1,8]
- In Canada, medetomidine has been identified in the unregulated opioid supply in Ontario and Quebec, and more recently in British Columbia.[9–11]
- In December 2025, a province-wide drug alert was issued after medetomidine was detected in over 30% of unregulated opioid samples in British Columbia.[13]
- Drug-checking programs continue to identify medetomidine in combination with fentanyl, benzodiazepines, and xylazine.[12]

Pharmacology

- Medetomidine is a racemic mixture of levomedetomidine and dexmedetomidine.[6]
- It is highly lipophilic and has high, selective affinity for α-2 adrenergic and imidazoline receptors.[14]
- Medetomidine induces sedation by inhibiting the release and metabolism of norepinephrine in the central nervous system.[15]

Clinical Challenge

- The isolated use of medetomidine is believed to be none or negligible at this time, as nearly all detected cases have been identified with illicit fentanyl exposure.
- Medetomidine overdose may result in profound central nervous system depression, hypotension, bradycardia, and respiratory depression that may not be fully reversible with naloxone.[17]
- Medetomidine withdrawal may emerge earlier than opioid or benzodiazepine withdrawal, with symptoms beginning within hours of last exposure.
- As a result, the withdrawal phenotype commonly overlaps with opioid and benzodiazepine withdrawal; medetomidine withdrawal should be suspected if hypertension, tachycardia, nausea, vomiting, or delirium persist despite treatment of either withdrawal syndrome.

Toxicity & Withdrawal

Clinical Manifestations of Medetomidine Toxicity in Fentanyl Contamination

Medetomidine toxicity in the context of fentanyl contamination can manifest as:

- Deep sedation or unresponsiveness
- Bradycardia
- Hypotension (or mixed hypertension–hypotension sequence)
- Respiratory depression not fully reversible by naloxone

Withdrawal Following Sustained Exposure to Medetomidine-Adulterated Fentanyl

Medetomidine withdrawal appears after sustained exposure through chronic use of contaminated fentanyl. Symptoms can begin within hours, commonly 4 to 6 hours after last exposure,[18] and can include:

- Marked hypertension and tachycardia
- Whole-body shivers without clonus or seizure
- Delirium, agitation, and confusion
- Nausea and vomiting
- Diaphoresis

Physiologic Basis and Severity of Medetomidine Withdrawal

These symptoms are consistent with central adrenergic hyperactivity, physiologically analogous to clonidine or dexmedetomidine withdrawal.[19] Case reports and series have further described severe medetomidine withdrawal with extreme tachycardia and hypertension, uncontrolled autonomic dysfunction, and accompanying shivers, anxiety, and protracted vomiting, which were often refractory to multiple agents and resulted in rapid deterioration within one to two hours.[20,21] Patients were also noted to be intolerable to oral medications due to excessive vomiting.

Distinctive Clinical Signals Associated with Medetomidine Exposure

Another defining feature of medetomidine in the literature is the occurrence of vivid and unexpected hallucinations.[22] Hallucinogenic effects, along with the sedation from α-2 adrenergic receptor agonists, may serve as unique signals to the presence of medetomidine in the unregulated market, analogous to the necrotic wounds observed with xylazine exposure.

Medetomidine Objective Withdrawal Scale (MOWS)

When to Initiate MOWS

Patients may be started on this protocol if all the following are met:

- Toxicology evidence with a urine drug screen or point-of-care test strip confirmation

OR

- History of known or suspected medetomidine exposure in acute withdrawal.

OR

- Unregulated fentanyl exposure.
- Presence of autonomic instability symptoms (e.g., hypertension, tachycardia, shivers) with alternative causes ruled out.

Causes may include but are not limited to stimulant intoxication, alcohol withdrawal, neuroleptic malignant syndrome, sepsis, acute coronary syndrome, pulmonary embolism.

Management Approach

In the context of an undifferentiated or combined withdrawal syndrome with risk for medetomidine withdrawal, opioid and benzodiazepine withdrawal should be managed in parallel throughout the clinical course.

Assess for opioid withdrawal

Follow institutional OW protocols utilizing full agonist opioids:

- Consider initiation and titration of Opioid Agonist Therapy if clinically indicated

Assess for benzodiazepine / alcohol withdrawal

If patient meets any of the following criteria, initiate CIWA-Ar[23] monitoring with PRN Lorazepam PO/SL/IV for scoring:

- Reported intentional benzodiazepine use separate from benzodiazepine-contaminated fentanyl (“benzo down”)
- History of benzodiazepine or alcohol withdrawal seizures
- Active alcohol use disorder

If none of the above are present, use a scheduled benzodiazepine taper without CIWA-Ar monitoring.

Benzodiazepine taper

Day 1: 1 mg Lorazepam PO/SL/IV QID

Day 2: 1 mg Lorazepam PO/SL/IV TID

Day 3: 1 mg Lorazepam PO/SL/IV BID

Day 4: 1 mg Lorazepam PO/SL/IV once daily

Day 5: Discontinue Lorazepam

Medetomidine withdrawal monitoring

Assess Medetomidine Objective Withdrawal Scale (MOWS) Q1H until MOWS < 3 for three consecutive readings, reduce scoring frequency to Q3H.

If MOWS remains < 3 for three consecutive Q3H scores, assess Q8H for 72 hours then discontinue protocol.

For any score greater than 3, restart protocol at Q1H.

Score the MOWS as per protocol.

Assign 1 point for each of the following observations:

- Heart rate > 110 bpm
- Systolic blood pressure > 160 mmHg
- Whole-body shivers
- Delirium/agitation
- Nausea or vomiting

At least one point from first two criteria met **and** total score ≥ 3 = clinically significant withdrawal

Medetomidine withdrawal treatment

First-line therapy: Clonidine

Scheduled Dosing

- 0.2 mg Clonidine PO TID for three days and then reassess (c*an be given buccal).*

Symptom Triggered

- Clonidine 0.2 mg PO q1h PRN, based on MOWS ≥ 3
- Maximum cumulative PRN dose in 6 hours: 1 mg
- Holding parameters: RR below 8, SpO2 less than 92%, HR below 60, BP below 95/65

Criteria for Escalation of Care and Consideration for Dexmedetomidine

- Cumulative PRN dose per 6 hours ≥1 mg
- Persistent delirium / severe agitation
- Autonomic instability (HR > 150 or BP > 200)
- Severe vomiting, with risk of compromised airway

Supportive Measures

In patients with nausea & vomiting and unable to drink fluids, yet are hypertensive, consider cautious, earlier IV fluid administration to reduce the risk of hypotension as blood pressure may drop quickly with treatment of the medetomidine withdrawal

Nausea Management

- Metoclopramide — 10 mg PO/IV q 6h PRN
- Olanzapine oral dissolving — 2.5–5 mg buccal HS PRN
- Ondansetron 4-8mg po/SL/IV q8h PRN
- Monitor for prolonged QTC with daily ECG

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