BRITISH COLUMBIA CENTRE ON SUBSTANCE USE

Concurrent Medetomidine-opioid Poisoning and Withdrawal Bulletin

Audience and Scope: This bulletin is primarily intended for physicians, nurses, nurse practitioners, and pharmacists providing care to people use who substances in acute, inpatient, and other monitored settings (e.g., withdrawal management). Limited considerations for outpatient and community settings are included.

Disclaimer: Given the dearth of evidence on this emerging concern, this bulletin is **based on limited published evidence and clinical experience and does not constitute a standard of care**. Clinicians are encouraged to use clinical judgement and consultation to guide care.

BCCSU
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1.0 Key Messages

Medetomidine is becoming a common adulterant in the opioid supply

- Medetomidine is an increasingly common non-opioid adulterant in BC's opioid supply, detected alongside fentanyl, other opioids, and benzodiazepines, and may worsen opioid toxicity through additional sedation.

Concurrent medetomidine and opioid poisoning may be atypical and protracted

- Naloxone should always be administered in the event of a suspected drug poisoning, as it will reverse the effects of opioids even if medetomidine is also present. However, naloxone does not reverse the effects of medetomidine, and there are currently no approved medications to reverse the effects of medetomidine in humans.

Patients who abruptly discontinue use of unregulated opioids are at risk of medetomidine withdrawal

- In those who have developed medetomidine dependence, withdrawal can occur within 4–6 hours of discontinuing opioids containing the adulterant medetomidine

It is important to recognize hallmark clinical presentations of co-occurring medetomidine and opioid poisoning and withdrawal

- Co-occurring medetomidine and opioid poisoning is characterized by opioid-induced respiratory depression responsive to naloxone, with prolonged sedation that is not responsive to naloxone. Additional features may include hypotension, persistent bradycardia, reduced airway protection, hyperglycemia, and hypothermia.
- The hallmark features of medetomidine withdrawal are tachycardia, profound hypertension, and vomiting that is often severe and non-responsive
  - Other common symptoms include tremors, diaphoresis, and hyperthermia

Medetomidine withdrawal is primarily treated with prompt administration of alpha-2 agonists (clonidine, dexmedetomidine)

- Alpha-2 agonists are the cornerstone of medetomidine withdrawal management, with clonidine being the most commonly used first-line treatment. Dexmedetomidine should only be utilized in severe or refractory cases, or if oral clonidine is not tolerated.

Medetomidine withdrawal can be a medical emergency

- Medetomidine withdrawal can progress rapidly and become life-threatening if left untreated. Early recognition, prompt treatment, and consultation with addiction medicine and/or toxicology are recommended.

2.0 Background

Medetomidine is an alpha-2 adrenergic agonist used in veterinary medicine for its sedative and analgesic properties. It is a 1:1 racemic mixture of dexmedetomidine and levomedetomidine, with dexmedetomidine representing the primary active enantiomer. As a sympatholytic agent, medetomidine reduces norepinephrine release, resulting in decreased heart rate and blood pressure. Similar to dexmedetomidine used in anesthesia, medetomidine may produce a biphasic cardiovascular response characterized by transient vasoconstriction and hypertension shortly after administration, followed by bradycardia and hypotension due to central sympathetic suppression; however, the initial hypertensive phase is not commonly observed in practice. At high doses, medetomidine becomes nonselective and activates imidazoline receptors leading to decreases in norepinephrine activity in the blood vessels, which causes bradycardia and initial hypertension, followed by hypotension. These effects are presumed to occur within the first 5–10 minutes following use and may be influenced by co-occurring substances such as opioids or stimulants.[1]

There is limited empirical data on the pharmacokinetics and pharmacodynamics of medetomidine in humans, particularly in the context of inhalational exposure through the unregulated drug supply. Animal data suggest effects may peak at approximately 30 minutes and last up to 4 hours, though this likely varies considerably depending on concentration, route of administration, and co-occurring substance exposure.[1]

Compared with xylazine, another veterinary sedative previously identified in the unregulated opioid supply, medetomidine is more than 100 times more potent and has approximately a 10-fold higher alpha2:alpha1 receptor selectivity ratio in animal studies. This greater alpha2 selectivity produces more profound sedation, analgesia, bradycardia, and hypotension, while reduced alpha1 activation may explain the lower rates of wound complications observed with medetomidine compared with xylazine.[2,3]

Medetomidine in the BC Context

Medetomidine emerged in the unregulated opioid supply in BC in 2024 and has rapidly increased in prevalence since that time. In fall 2025, BC saw a marked rise in drug poisonings attended by paramedics and in March 2026 recorded the highest total paramedic-attended drug poisoning events[a] (50.04 per 100,000).[4,5] Clinicians in BC are increasingly reporting opioid poisonings with signs suggestive of concurrent medetomidine involvement, including profound and prolonged sedation and bradycardia.

Medetomidine is commonly detected alongside fentanyl, other opioids, and benzodiazepines. Secondary opioid testing in BC has identified a rapid increase in medetomidine detections over the past year, with medetomidine found in 49.1% of samples undergoing secondary testing in January 2026 (note: this figure does not represent the prevalence of medetomidine across all opioid samples tested).[6] Conversely, xylazine prevalence has sharply declined and is now detected in less than 1% of samples. Similar trends have been observed nationally and internationally, including in Toronto where drug-checking data found medetomidine in 85% of all opioid samples recently tested in February 2026[7]; With an over 90% [DT1] increase in medetomidine-adulterated samples in Toronto from 2024 (27%; 289 of 1,071 samples) to 2025 (52%; 549 of 1,062 samples).[8,9]

Importantly, prevalence data do not reflect the concentration of the drug. In March 2026, secondary testing across BC found concentrations ranged from <1% to 16%, with the median being 1.7%.[10] In comparison, Philadelphia has been at the forefront of managing medetomidine adulteration in the United States, where average medetomidine concentrations increased from less than 3% in Q2 2024, when it was first detected, to approximately 15% by Q4 2025.

a. Paramedic-attended drug poisonings may include unconfirmed drug poisonings, double counting if there are 2 phone calls (or not counted at all if someone flags down an ambulance), and do not include demographic data.

3.0 Identifying Concurrent Medetomidine and Opioid Poisonings

In BC, medetomidine is almost always detected alongside fentanyl, other opioids, and benzodiazepines. This results in a mixed clinical presentation, with medetomidine contributing additional sedation that may worsen opioid toxicity and make it difficult to distinguish the individual effects of each substance.[b] However, because medetomidine is not detected in routine urine drug screens or standard toxicology panels, **recognition is largely based on clinical presentation.**[11-13]

Clinical effects from poisonings may include[6,11,13]**:**

- Opioid-induced respiratory depression (responsive to naloxone)
- Severe prolonged sedation that is not reversed by naloxone
- Hypotension, sometimes preceded by brief hypertension
- Severe bradycardia, often lasting longer than hypotension
- Reduced airway protection
- Increased blood glucose
- Decreased body temperature

Effects may last from 90 minutes to several hours or longer:

- Bradycardia commonly lasts 3–9 hours
  - Some cases persist even after blood pressure normalizes or hypertension develops
- Although medetomidine may initially cause transient hypertension, this phase is rarely observed in clinical practice
  - This is thought to be due to its short duration, early onset after exposure, and the potential for its effect to be masked by opioids or other co-occurring adulterants

Concurrent medetomidine-involved poisoning should be suspected in patients with atypical presentations for opioid poisoning, including bradycardia and prolonged sedation that is not responsive to naloxone.

b. While medetomidine adulteration has resulted in increased need for medical intervention, there is no evidence of increased drug poisoning deaths related to this trend.

4.0 Managing Concurrent Medetomidine and Opioid Poisoning

Naloxone should always be administered in the event of a drug poisoning as it can reverse the effects of opioids and restore breathing.

- Titrate naloxone cautiously, aiming to restore respiratory rate; wakefulness may not be an appropriate target in true medetomidine intoxication
  - Note: If the patient is breathing adequately, avoid excessive dosing of naloxone. High naloxone dosing could provoke opioid withdrawal in a patient who remains sedated by alpha-2 agonists, leading to emesis and risk of aspiration
- Repeat doses may be necessary while supporting patients through medetomidine poisoning

There is currently no approved reversal agent for human use for medetomidine poisoning. Although atipamezole is used in veterinary medicine, it has not been tested in humans and is considered unsafe due to the risk of severe withdrawal-like reactions. Similarly, yohimbine is another potential reversal agent due to its alpha-2 antagonism. However, although it is used in humans, it is not approved for reversing the effects of medetomidine,[14] and prescription-strength yohimbine is no longer available in Canada.

Following recognition of possible medetomidine involvement, management should be guided by the patient's clinical presentation and symptom severity. For the vast majority of patients, observation and supportive care are sufficient. Potential management strategies may include[11-13]:

- Monitoring, including heart rate and blood pressure
- Airway management and respiratory support
  - Most patients do not require advanced airway intervention; approximately 30% of hospitalized cases in Philadelphia have required intensive care unit (ICU)-level monitoring and supportive care[15]
- Warming measures for hypothermia
- IV fluids
- In exceptional circumstances, vasopressors for hypotension
- Avoid atropine for isolated bradycardia unless there is impending cardiac arrest; titratable inotropes (e.g., dobutamine or isoproterenol) are preferred if intervention is needed

5.0 Identifying Medetomidine-opioid Withdrawal

Repeated medetomidine exposure may rapidly lead to dependence and severe withdrawal symptoms, which may further reinforce ongoing use to avoid withdrawal. However, given the limited empirical data, it is unclear how quickly medetomidine dependence begins.

What we know about medetomidine withdrawal[16–18]

- Repeated use of medetomidine can lead to physical dependence and withdrawal
- Development of physical dependence may occur within 1–2 weeks or less, depending on the frequency and intensity of use
- Withdrawal symptoms may emerge within hours of discontinuation
  - Transition from intoxication to withdrawal may be rapid, often occurring within 4–6 hours (or even more rapidly), with symptoms escalating from minimal dysphoria to severe autonomic dysfunction over time[19]
  - Can occur in hospital, community, or withdrawal management settings
  - May also emerge due to fluctuations in the unregulated drug supply, such as changes in suppliers or adulterant concentrations
- Medetomidine withdrawal can cause metabolic abnormalities such as hypokalemia that may contribute to QTc prolongation
- Other complications from medetomidine withdrawal include encephalopathy and stress-induced cardiomyopathy from myocardial injury[20]
- Clinical presentations may be further complicated by co-occurring benzodiazepine withdrawal, which may also be due to unintended exposure from adulterated drugs

What we know about dexmedetomidine withdrawal from the literature[21,22]

Note: Dexmedetomidine is the active enantiomer of medetomidine. In the absence of sufficient data relating to the unregulated drug supply, information on dexmedetomidine withdrawal derived from ICU studies represents the best available evidence regarding alpha-2 agonist dependence and withdrawal as of June 2026.

- Withdrawal symptoms have been reported in approximately one-third of patients receiving dexmedetomidine infusions for more than 2–3 days
- Retrospective ICU studies found withdrawal symptoms in:
  - Approximately 30% of patients after as little as 24 hours of exposure
  - Approximately 35% of patients after 72 hours or longer of exposure
- Withdrawal observed in ICU settings is generally milder than severe withdrawal symptoms reported with medetomidine-adulterated opioids

- In critical care settings, clonidine is commonly used to facilitate weaning from dexmedetomidine
  - There is limited experience using high-dose alpha-2 agonist therapy outside critical care settings
  - Clonidine is typically tapered and discontinued before hospital discharge
  - A limited literature search suggests dexmedetomidine is approximately 8 times more selective toward alpha-2 receptors than clonidine[23]
- These dosing regimens are generally initiated in highly monitored ICU settings, where patients have:
  - Continuous telemetry
  - Frequent vital sign monitoring
  - Skilled nursing support
  - Concurrent sedative medications

Table 1. Common and Less Common Features of Medetomidine Withdrawal[3,18,20,24-26]

Hallmark Symptoms of Medetomidine Withdrawal	

• Marked sympathetic hyperactivity, including tachycardia (e.g., 100–150 bpm)
• Severe hypertension (e.g., >200/120 mm Hg) may appear within 4–6 hours of last use
• Severe nausea and vomiting
  ◦ Often non-responsive to traditional anti-emetics
  ◦ More pronounced than with fentanyl withdrawal
  ◦ Often coincides with rising heart rate and blood pressure	

Common Features of Medetomidine Withdrawal	**Less Common Features of Medetomidine Withdrawal**

• More rapid onset and faster deterioration compared to opioid withdrawal
• Does not respond to full opioid agonists
• Hallucination
• Intense agitation, restlessness
• Diaphoresis
• Mydriasis
• Disordered movements
  ◦ Hypokinesis
  ◦ Myoclonus
  ◦ Dystonia/dystonic posturing
  ◦ Athetosis (slow, involuntary, convoluted, writhing movements of the fingers, hands, toes, and feet)
• Coarse tremor (jaw) without clonus or hyper reflexivity
• Potentially accompanied by features of typical opioid withdrawal, where:
  ◦ Clinical Opiate Withdrawal Scale (COWS) score may be lower because of hypokinesis, mutism, or both; or higher due to non-specific medetomidine withdrawal symptoms
	• Mutism
	• Cardiac arrest
	• Pseudo catatonia
	• Hyperthermia
	• Hiccups
	• Risk of aspiration, esophageal tears (Mallory-Weiss syndrome) are possible
	• Biphasic delirium, often starts as agitation and often progresses to hypo active encephalopathy
	• "Brain zaps," described by patients as similar to SSRI/SNRI withdrawal: sudden electrical feeling or jolt, sometimes accompanied by dizziness/light headedness
	• Urinary retention
	• Posterior reversible encephalopathy syndrome (PRES)—acute neurovascular disorder characterized by seizures, encephalopathy, headache, visual disturbances—typically occurring alongside rapidly rising blood pressure
	• Seizures (rarely seen)
	  ◦ Seizures are not reliably attributed to medetomidine, given other adulterants in the unregulated drug supply (e.g., benzodiazepines)

Medetomidine withdrawal may share some clinical features with benzodiazepine withdrawal; however, prominent sympathetic hyperactivity (e.g., severe hypertension, tachycardia, diaphoresis, and hyperthermia) and limited response to benzodiazepines or phenobarbital can help distinguish the syndrome.	

Table 2. Opioid, Medetomidine, and Overlapping Withdrawal Signs and Symptoms

Opioid Withdrawal	Overlapping Signs and Symptoms	Medetomidine Withdrawal
○ Piloerection ○ Lacrimation/rhinorrhea ○ Diarrhea ○ Yawning	○ Tachycardia ○ Hypertension ○ Nausea and vomiting ○ Tremor ○ Agitation/anxiety ○ Diaphoresis ○ Myalgia ○ Mydriasis	○ Course jaw tremor ○ Muscle contraction/dystonia ○ Hypoactive mental status ○ Hiccups
Onset: More gradual		Onset: Rapid
Responds to full opioid agonists		Does not respond to full opioid agonists

6.0 Managing Concurrent Medetomidine and Opioid Withdrawal

As of June 2026, only opioid-positive samples have been found to be adulterated with medetomidine. Consequently, clinical experience suggests that medetomidine withdrawal almost always co-occurs with opioid withdrawal and both syndromes should be managed simultaneously.

6.1 Managing Opioid Withdrawal

Medetomidine withdrawal may precede severe opioid withdrawal and may interfere with obtaining accurate COWS scores. It is essential to treat opioid withdrawal as well as medetomidine withdrawal.[20,27] Treatment with alpha-2 agonists is covered in the section below on managing medetomidine withdrawal.

- Concurrent opioid withdrawal should be treated with short-acting opioids, initiation or continuation of opioid agonist treatment (OAT), or both[16,18]
  - **Most effective when OAT and short-acting opioids are used in combination**
  - Titrate to resolve opioid withdrawal symptoms
- **Opioid agonist treatment**
  - Methadone
  - Slow-release oral morphine (SROM)
  - Buprenorphine/naloxone
    - Patients already stabilized on buprenorphine/naloxone should continue treatment
    - If buprenorphine/naloxone induction is preferred by the patient and clinically appropriate:
      - Traditional inductions may be challenging given the difficulty in using COWS scores to assess withdrawal severity, and precipitated withdrawal may worsen autonomic instability
      - Low-dose inductions may be preferred if medetomidine withdrawal symptoms are controlled, but should be undertaken with caution and expert consultation, as appropriate
- **Short-acting opioids**
  - Hydromorphone or morphine
    - If unable to tolerate oral treatment utilize IV methods

Clinicians are encouraged to follow guidance from the *Guideline for the Clinical Management of Opioid Use Disorder Guideline (2023)* for managing opioid withdrawal and initiating OAT.

6.2 Managing Medetomidine Withdrawal

This guidance is primarily intended for inpatient settings such as hospital settings where IV medetomidine and enhanced monitoring is available. While inpatient care is strongly encouraged, it is recognized that there may be situations in which monitored withdrawal management and outpatient care may be the only feasible approach for certain scenarios. In these cases, please refer to the specific monitored withdrawal management and outpatient management section in this document.

Overview

Early addiction medicine and/or toxicology consultation is recommended for suspected medetomidine withdrawal

Withdrawal Management

- **Alpha-2 agonists are the cornerstone of medetomidine withdrawal management,** with clonidine being the most commonly used first-line treatment
  - Should be initiated as soon as possible if medetomidine withdrawal is suspected based on patient's condition, ideally during the transition from intoxication to withdrawal
  - **In most patients, withdrawal can be successfully managed with clonidine and anti-emetics**, particularly when withdrawal is recognized and treated early
  - **Higher doses than usual are typically needed to achieve symptom relief, and standardized best practices have not yet been established**
  - With appropriate and prompt treatment, most patients do not require ICU-level support
- Patients with sustained hemodynamic instability, severe agitation, decreased level of consciousness, withdrawal complications, or refractory symptoms may require transfer to a higher level of care for IV dexmedetomidine and close monitoring
  - Inability to tolerate oral medications alone is not necessarily an indication for ICU transfer and should be assessed in the context of overall clinical status
- Once stabilized on dexmedetomidine, **oral clonidine can be initiated as a cross-taper to facilitate weaning from the infusion**
- Potential alternatives to clonidine include guanfacine and tizanidine; however, these are utilized far less often

Supportive Care

- Supportive care should be guided by clinical presentation and is often focused on managing **severe nausea and vomiting**, which is important for facilitating oral clonidine administration and enhancing patient comfort
- Clinical experience suggests that **dopamine antagonists (e.g., prochlorperazine, olanzapine)** may be more effective than traditional anti-emetics for withdrawal-related nausea and vomiting
- Monitor for **QTc prolongation**, particularly when using the above anti-emetics or in patients with electrolyte abnormalities or other risk factors

The following sections provide more detailed information on management strategies, including clinical experience on dosing, where available.

6.2.1 Clonidine[28]

Clonidine is considered first-line treatment for most individuals. If unable to tolerate oral, consider using sublingual administration of oral tablet.

- Mechanism: Central alpha-2 adrenergic receptor agonist that reduces norepinephrine release, decreasing sympathetic outflow
- Effect on blood pressure: Lowers blood pressure and heart rate by reducing sympathetic nervous system activity
- Time to peak effect (oral formula): Approximately 2–4 hours
  - May not yet see peak effects if doses are given hourly
- Onset of action: Usually within 30–60 minutes
- Half-life: Approximately 6–20 hours
  - May be prolonged for people with renal dysfunction
- Duration of effect: ~8 hours

6.2.1.1 Considerations[27,29]:

- For patients with suspected medetomidine withdrawal, particularly those with marked hypertension and tachycardia that are disproportionate to expected opioid withdrawal symptoms:
  - Initial doses of oral clonidine range between 0.2–0.6 mg,[c] guided by vital signs and symptoms severity, though higher doses may be necessary to control withdrawal[29]
    - Other causes of autonomic hyperactivity (e.g., serotonin syndrome, traumatic brain injury, subarachnoid hemorrhage, sepsis) should be excluded before initiating and rapidly escalating to high dosing regimens
  - Loading doses are typically administered q2–4h (up to 3 doses) until symptoms improve
    - Followed by similar or decreased doses q4–6h, as part of a scheduled taper
  - **Note: The clonidine dosages used to manage medetomidine withdrawal are significantly higher than recommended for other withdrawal presentations (e.g., opioids, alcohol) and could be harmful for individuals who are not experiencing medetomidine withdrawal. These regimens should be individualized and patients closely monitored, as patients without medetomidine withdrawal may be at increased risk of hypotension, bradycardia, sedation, and other adverse events. Careful assessment is therefore essential before initiating high-dose clonidine therapy.**
- **Where hypotension is a concern (e.g., sepsis):**
  - Use a lower test dose and more frequent monitoring
  - Consider critical care/high acuity admission
- If individuals are not sufficiently responding to the upper end of dosing described above, clinicians should concurrently explore potential ICU transfers, if necessary
- Clonidine should generally be tapered over 5-7 days
  - In rare cases, some patients may require prolonged outpatient taper over several weeks, or months; however, there are harms associated with longer tapers and this should be used as a last resort[30]
    - Patient counseling on tapers should ideally be discussed before initiation
  - This is to minimize rebound symptoms, withdrawal recurrence, and dependence
  - Close follow-up and blood pressure monitoring are required[18,29]
- Clonidine tablets can be used sublingually in those with ongoing nausea and vomiting, although absorption may be incomplete,[31] making accurate dosing challenging to assess
- Patients should be counseled to stop taking clonidine if they return to non-prescribed substance use; however, patients should also be advised of the risk of rebound hypertension if clonidine is abruptly discontinued
  - Clonidine poisoning can present with a similar pattern as opioid poisoning (bradycardia, hypotension, decreased level of consciousness, confusion, miosis, respiratory depression) and this medication should be dosed with caution, especially if being used in the outpatient setting

c. Given the limited data on medetomidine withdrawal, dosing recommendations are based on consensus rather than evidence-based recommendations and clinical guidance, and there are variations in reported dosages across publications. For example, META:PHI's suggested dosing for oral clonidine is 0.3–0.9 mg every 1–2 hours until vital signs improve and withdrawal symptoms stabilize.

6.2.2 Dexmedetomidine[32]

- Mechanism: Highly selective alpha-2 adrenergic receptor agonist that decreases central sympathetic outflow, producing sedation, anxiolysis, analgesia, and reduced norepinephrine release with minimal respiratory depression
- Effect on blood pressure: Typically lowers blood pressure and heart rate through central sympatholytic action
- Time to peak effect: Approximately 15–30 minutes after IV administration
- Onset of action: 5–10 minutes after IV administration
- Half-life: Approximately 2 hours
- Duration of effect: 30–60 minutes after discontinuation

Intravenous dexmedetomidine should be considered for severe or refractory cases, and when patients cannot tolerate oral clonidine[27,33]

- Clinical experience has found that dexmedetomidine plus high-dose clonidine (0.4–0.6 mg oral) along with aggressive and early anti-emetics (i.e., olanzapine, prochlorperazine) are the most effective interventions for managing severe medetomidine-opioid withdrawal
- Some settings require transfer to ICU for dexmedetomidine, while others allow its use in the emergency department; in all cases, dexmedetomidine requires critical care-trained providers
- Patients should transition to oral clonidine after stabilization
  - Clonidine remains the preferred oral alpha-2 adrenergic agonist
  - Alternative agents such as guanfacine have been described when clonidine is poorly tolerated, although evidence is limited
- Dexmedetomidine infusions can generally be discontinued after 24–48 hours as withdrawal symptoms decrease[3]

6.2.2.1 Considerations[34-36]:

- Cardiac monitoring is required
- Once stabilized (usually 24–48 hours), cross-taper to clonidine along with supportive care as needed
- Infusions are typically initiated at 0.5 mcg/kg/h and adjusted by 0.1 to 0.2 mcg/kg/h every 15 to 30 minutes based on clinical response (e.g., heart rate, blood pressure, and COWS score)
- Most patients require infusion rates between 0.5 and 1.5 mcg/kg/h
- Dexmedetomidine contraindications:
  - Heart rate <50 bpm
  - MAP <65 mm Hg
  - 2nd or 3rd degree heart block

6.3 Managing Severe Nausea and Vomiting

Dopamine antagonists are preferred for medetomidine-associated withdrawal symptom control, particularly severe nausea and vomiting. Suggested dosing information is provided below:

- Metoclopramide* (oral/SC/IM/IV): 5–10 mg q4–6h PRN
  - Note: Dose adjustment may be required for patients with renal impairment
- Haloperidol* (dosing differs by route)
  - Oral: 0.5–1 mg q6h PRN
  - IM/SC: 0.5–2 mg q6–8h PRN
  - IV: 1 mg q6h PRN
    - IV dose must be intermittent (not direct)
    - Advanced monitoring required for IV
  - Considerations:
    - Suggested maximum daily dose of 20 mg
    - Greater risk of QTc prolongation
      - Risk is higher at higher doses, with IV administration, and with other QTc prolongation risk factors
    - Can be sedating for patients
    - Monitor for extrapyramidal symptoms (EPS), especially in young, male, antipsychotic naïve patients
- Olanzapine*† (oral*/oral dissolving tablet/IM): 2.5–5 mg q8h PRN
  - Suggested maximum daily dose of 10 mg
  - Can be sedating for patients
  - **Use caution** if administering IM olanzapine concurrently with parenteral benzodiazepines, as this combination may increase the risk of excessive sedation and respiratory depression
- Prochlorperazine* (oral/rectal): 5–10 mg q4h PRN up to a maximum of 40 mg per day
- **Clinicians are encouraged to consult the BC Drug and Poison Centre for advice on the management of challenging cases**

***Caution if QTc greater than 500**
†Requires advanced monitoring

6.3.1 Managing Severe Hypertension[24,33]

If severe hypertension persists despite treatment with alpha-2 agonists, clinicians may opt to treat with short-acting antihypertensives, as progression to hypertensive emergency is possible in severe withdrawal.
However, hypertension should be managed as part of the broader withdrawal syndrome rather than as an isolated phenomenon, with antihypertensives often used as a temporary bridge while initiating clonidine or as an adjunct after dexmedetomidine infusion has reached maximum dosing.

Considerations:

- Management should account for whether maximal alpha-2 agonist therapy has been reached and whether other withdrawal symptoms are adequately controlled
- Easily titratable intravenous agents, including esmolol, labetalol, or hydralazine, are generally preferred when oral therapy is not tolerated

6.4 Monitored Withdrawal Management

Medetomidine withdrawal may occur in monitored withdrawal management settings and patients may present with significant autonomic symptoms requiring prompt recognition and individualized management. Treatment should be guided by symptom severity, clinical stability, and the level of monitoring available, with early recognition of severe or worsening symptoms that warrant escalation to a higher level of care

- The management strategies outlined above should be utilized; however, dexmedetomidine is not available without transfer to a hospital/ICU

Although monitored withdrawal management settings can support management of mild-to-moderate withdrawal symptoms, some patients with medetomidine withdrawal may require transfer to an acute care or inpatient setting due to the severity of autonomic instability, need for intensive monitoring, or complexity of care.
Consider escalation to higher-level care when:

- There is persistent or worsening hypertension, tachycardia, agitation, or autonomic hyperactivity despite appropriate clonidine titration
- There is concern for hypotension, bradycardia, profound nausea and vomiting, decreased level of consciousness, or respiratory compromise
- There is diagnostic uncertainty or concern for alternative causes of severe autonomic instability (e.g., serotonin syndrome, sepsis)
- Symptoms require clonidine doses beyond what can be safely monitored in the withdrawal management setting
- The patient requires interventions (e.g., dexmedetomidine), monitoring, or medical supports unavailable in the withdrawal management setting
- There are significant concurrent medical or psychiatric concerns requiring inpatient management

6.5 Outpatient Management

Outpatient management of medetomidine withdrawal in individuals with features of or at risk of severe withdrawal (i.e., tachycardia, hypertension, hemodynamic instability) should generally be avoided, with inpatient management strongly encouraged unless infeasible (e.g., patient refusal, rural and remote settings with barriers to travelling for inpatient care).

In these limited scenarios, the following is suggested **in the outpatient setting:**

- Management should be individualized based on patient characteristics, clinical stability, and ability to engage in close follow-up
- Concurrent opioid withdrawal should be treated with initiation or continuation of OAT, short-acting opioids
  - In this context, short-acting opioids are subject to witnessed dosing as per the BC Ministry of Health's *Access to Prescribed Alternatives in British Columbia: Policy Direction*
  - Clinicians are encouraged to follow guidance from *A Guideline for the Clinical Management of Opioid Use Disorder Guideline (2023)* for initiating and continuing OAT
  - For additional support managing opioid withdrawal in the context of co-occurring medetomidine withdrawal, consult the 24/7 Addiction Medicine Clinician Support Line (778-945-7619)
- Clonidine may be used for symptom management
  - Initiated at 0.1–0.3 mg TID or QID
    - A baseline blood pressure test in clinic is necessary before prescribing clonidine
    - Note: The clonidine dosages used to manage medetomidine withdrawal are significantly higher than recommended for other withdrawal presentations (e.g., opioids, alcohol) and could be harmful for individuals who are not experiencing medetomidine withdrawal, especially in the context of limited monitoring available in outpatient management
  - Should only be used when patients are **not continuing to use unregulated CNS depressants**
    - Concurrent use may increase risk of excessive sedation, CNS depression, severe hypotension, bradycardia
    - Counsel patient to stop clonidine use if they do return to unregulated CNS depressant use
  - Clonidine is a regular benefit covered by BC PharmaCare
- Ideally, patients should be equipped with a home blood pressure monitor to facilitate frequent systolic blood pressure monitoring and counselled to avoid taking these medications if their blood pressure is low (systolic blood pressure less than 120 mm Hg)
  - Suggested blood pressure monitoring:
    - Baseline (pre-dose); q30–60 min following first dose; then q2–4h based on prescriber's advice on patient reaction to first several doses
- Nausea and vomiting can be managed with dopamine antagonists; however, they should be used with caution. Intractable vomiting or escalating doses indicate the patient should be transferred to a higher level of care
  - See *Managing Severe Nausea and Vomiting* for dosing information
- Close clinical follow-up and ongoing support are required
  - Consider recommending a support person to help check-in on the patient and bring them to clinical care, if needed
- Patients should be counselled to seek urgent medical assessment or present to the emergency department if:
  - Withdrawal symptoms worsen
  - Severe vomiting, chest pain, or other withdrawal symptoms develop

Early addiction medicine and/or toxicology consultation is recommended for suspected medetomidine withdrawal.

Clinicians are encouraged to consult the **24/7 Addiction Medicine Clinician Support Line** (778-945-7619) or the **RACE App** to discuss any concerns with managing withdrawal symptoms.

7.0 Additional Resources

British Columbia Centre on Substance Use: Medetomidine

Canadian Centre on Substance Use and Addiction: CCENDU Drug Alert: Medetomidine Detected in Canada's Unregulated Drug Supply

BC Centre for Disease Control: Medetomidine: Substance Information Sheet

Philadelphia Department of Public Health: Medetomidine: What you need to know about the new street drug taking over Philly

References

1. Vancouver Coastal Health. Medetomidine in the unregulated drug supply. 2024. Accessed May 26, 2026. https://www.vch.ca/en/media/35801
2. Virtanen R, Savola J-M, Saano V, Nyman L. Characterization of the selectivity, specificity and potency of medetomidine as an alpha 2-adrenoceptor agonist. European journal of pharmacology. 1988;150(1-2):9-14. doi:10.1016/0014-2999(88)90744-3
3. Zimmerman DE, Goodstein D, Durney PA, Patel-Francis SH, London KS. Presentation and management of acute medetomidine withdrawal. American journal of health-system pharmacy. 2026;doi:10.1093/ajhp/zxag141
4. BC Centre for Disease Control. Paramedic-Attended Overdose Event Rate and Unregulated Drug Death Rate in British Columbia. Data provided by BCEHS and BCCS. Extracted on April 16, 2026.
5. BC Centre for Disease Control. Unregulated Drug Poisoning Emergency Dashboard. 2026. https://www.bccdc.ca/health-professionals/data-reports/substance-use-harm-reduction-dashboard
6. BC Centre on Substance Use. Medetomidine, xylazine, and carfentanil detected via secondary testing. 2026. Accessed May 26, 2026. https://drugcheckingbc.ca/
7. Service TsDC. Unregulated fentanyl supply trends: Toronto, Ontario (February 7-20, 2026) [Internet]. 2026. https://drugchecking.community/wp-content/uploads/dlm_uploads/2026/02/Torontos-Drug-Checking-Service-report_Feb7-20-2026.pdf
8. Toronto's Drug Checking Service. Veterinary tranquilizers found in expected fentanyl samples. Graphs. 2026. https://drugchecking.community/
9. Public Health Agency of Canada. Drug Analysis Service. Analyzed Drug Report. 2026. https://health-infobase.canada.ca/drug-analysis-service/analyzed-drug-report.html
10. BC Centre on Substance Use. Drug Checking in British Columbia March 2026. https://drugcheckingbc.ca/wp-content/uploads/sites/4/2026/05/Drug_Checking_BC_Mar_2026.pdf
11. BC Centre for Disease Control. Medetomidine: substance information sheet. BC Centre for Disease Control. 2024. Accessed May 26, 2026. https://www.bccdc.ca/resource-gallery/Documents/Harm%20Reduction/Medetomidine%20Substance%20Info%20Sheet.pdf
12. Krotulski AJ SJ, Moraff C, Wood T, Walton S, Debord J, Denn M, Quinter A, Logan BK. Medetomidine rapidly proliferating across USA—implicated in recreational opioid drug supply and causing overdose outbreaks. Centre for Forensic Research and Education. 2024. Accessed May 26, 2026. https://www.cfsre.org/nps-discovery/public-alerts/medetomidine-rapidly-proliferating-across-usa-implicated-in-recreational-opioid-drug-supply-causing-overdose-outbreaks
13. Palamar JJ, Krotulski AJ. Medetomidine Infiltrates the US Illicit Opioid Market. JAMA : the journal of the American Medical Association. 2024;332(17):1425-1426. doi:10.1001/jama.2024.15992
14. Talukder MH, Hikasa Y, Takahashi H, Sato K, Matsuu A. Antagonistic effects of atipamezole and yohimbine on medetomidine-induced diuresis in healthy dogs. Canadian journal of veterinary research. 2009;73(4):260-270.
15. Philadelphia Department of Public Health, Division of Substance Use Prevention and Harm Reduction. Medetomidine. 2025. Accessed May 26, 2026. https://www.substanceusephilly.com/medetomidine
16. London KS, Huo S, Murphy L, et al. Severe Fentanyl Withdrawal Associated With Medetomidine Adulteration: A Multicenter Study From Philadelphia, PA. Journal of addiction medicine. 2026;20(2):231-237. doi:10.1097/ADM.0000000000001560
17. Lynch MJ, Pizon AF, Yealy DM. Emergence of Medetomidine in the Illicit Drug Supply: Implications for Emergency Care and Withdrawal Management. Annals of emergency medicine. 2026;doi:10.1016/j.annemergmed.2025.12.004
18. Penn Center for Addiction Medicine and Policy. ICU Medetomidine-fentanyl Withdrawal Management Strategy. 2025. Accessed May 26, 2026. https://penncamp.org/wp-content/uploads/2025/09/Opioid-with-Suspected-Adulterant-Withdrawal-ICU-Protocol_REVISION_7.2025.docx
19. Ostrowski SJ, Tamama K, Trautman WJ, Stratton DL, Lynch MJ. Notes from the Field: Severe Medetomidine Withdrawal Syndrome in Patients Using Illegally Manufactured Opioids — Pittsburgh, Pennsylvania, October 2024–March 2025. MMWR Morbidity and mortality weekly report. 2025;74(15):269-271. doi:10.15585/mmwr.mm7415a3
20. Huo S, London K, Murphy L, et al. Notes from the Field: Suspected Medetomidine Withdrawal Syndrome Among Fentanyl-Exposed Patients — Philadelphia, Pennsylvania, September 2024–January 2025. MMWR Morbidity and mortality weekly report. 2025;74(15):266-268. doi:10.15585/mmwr.mm7415a2

21. Kim CS, McLaughlin KC, Romero N, Crowley KE. Evaluation of Dexmedetomidine Withdrawal and Management After Prolonged Infusion. Clinical therapeutics. 2024;46(12):1034-1040. doi:10.1016/j.clinthera.2024.09.006
22. Pathan S, Kaplan JB, Adamczyk K, Chiu SH, Shah CV. Evaluation of dexmedetomidine withdrawal in critically ill adults. Journal of critical care. 2021;62:19-24. doi:10.1016/j.jcrc.2020.10.024
23. Kamibayashi T, Maze M, Weiskopf Richard B, Weiskopf Richard B, Todd Michael M. Clinical Uses of α2-Adrenergic Agonists. Anesthesiology. 2000;93(5):1345-1349. doi:10.1097/00000542-200011000-00030
24. Sibley AL, Bedard ML, Tobias S, et al. Emergence of Medetomidine in the Unregulated Drug Supply and Its Association With Hallucinogenic Effects. Drug and alcohol review. 2025;44(7):1896-1906. doi:10.1111/dar.70024
25. Murphy L, Krotulski A, Hart B, Wong M, Overton R, McKeever R. Clinical characteristics of patients exposed to medetomidine in the illicit opioid drug supply in Philadelphia – a case series. Clinical toxicology (Philadelphia, Pa). 2025;63(6):438-441. doi:10.1080/15563650.2025.2500601
26. Philadelphia Department of Public Health. Health alert: medetomidine as an emerging adulterant in the illicit drug supply. 2024. Accessed Jul7 7, 2026. https://hip.phila.gov/document/4874/PDPH-HAN-00444A-12-10-2024.pdf
27. Zhu DT, Palamar JJ. Responding to medetomidine: clinical and public health needs. Lancet Regional Health - Americas (Online). 2025;44:101053-101053. doi:10.1016/j.lana.2025.101053
28. Patel P, Saadabadi A. Clonidine. Treasure Island (FL): StatPearls Publishing. 2026. Accessed Accessed June 10, 2026. https://www.ncbi.nlm.nih.gov/books/NBK459124/
29. META:PHI. Medetomidine: Emerging Adulterant in the Drug Supply. META:PHI Webinar. 2026. Accessed May 26, 2026. https://www.metaphi.ca/wp-content/uploads/SpecialWebinar_Medetomidine_26.02.18.pdf
30. META:PHI. Emerging Practice: Medetomidine Combined Fentanyl/Medetomidine Withdrawal in the Ambulatory Setting. 2026. https://www.metaphi.ca/wp-content/uploads/MedetomidineOpioidWithdrawal_Ambulatory.pdf
31. META:PHI. Emerging Practice: Medetomidine Combined Fentanyl/Medetomidine Withdrawal in the ED/Acute Care Setting. 2026. https://www.metaphi.ca/wp-content/uploads/MedetomidineOpioidWithdrawal_ED.pdf
32. Pfizer Canada ULC. Precedex Product Monograph. December 9, 2009. Updated August 30, 2024. Accessed July 7, 2026. https://webfiles.pfizer.com/file/6d973198-b241-4a86-9a22-a8ec0d17fed9?referrer=ccb731e5-4f2d-4f4a-b2dc-e5e912145fc6
33. Penn Center for Addiction Medicine and Policy. Medetomidine. 2025. Accessed May 26, 2026. https://penncamp.org/medetomidine/
34. Iirola T, Aantaa R, Laitio R, et al. Pharmacokinetics of prolonged infusion of high-dose dexmedetomidine in critically ill patients. Critical care (London, England). 2011;15(5):R257-R257. doi:10.1186/cc10518
35. Van Berkel Patel M, Bolton S, Hamilton C. Standard- versus High-Dose Dexmedetomidine for Sedation in the Intensive Care Unit. Hospital pharmacy (Philadelphia). 2022;57(2):281-286. doi:10.1177/00185787211029552
36. Voscopoulos C, Kirk FL, Lovrincevic M, Lema M. The use of "High Dose" Dexmedetomidine in a Patient with Critical Tracheal Stenosis and Anterior Mediastinal Mass. The open anesthesiology journal. 2011;5(1):42-49. doi:10.2174/1874321801105010042