

# OVERDOSE RESPONSE CENTER

## Partner Information Bulletin

#2026-03

### CLINICAL GUIDANCE: MEDETOMIDINE



#### Overview

- Delaware's Overdose System of Care, with support from the Overdose Response Center, is sharing the following clinical recommendations for addressing medetomidine, currently being seen across the state's medical systems.
- Medetomidine has been increasingly detected in Delaware's illicit drug supply, and is expanding throughout the state.
- The following pages provide targeted clinical guidance to a variety of settings (outpatient, ED, in hospital).

#### Background

- Medetomidine is an alpha-2-adrenergic agonist medication approved for veterinary use only.
- In early 2024 medetomidine was detected in the street drug supply in Philadelphia, followed by a rapid increase in the number and severity of overdoses in Philadelphia and northern Delaware.
- Unlike opioid-only overdoses, medetomidine causes profound **bradycardia** and **sedation** that does not respond to naloxone, though naloxone remains vital for the reversal of concurrent opioid-induced respiratory depression.
- Severe withdrawal syndromes have caused large increases in hospital admissions, including in the Philadelphia and northern Delaware areas.

#### Medetomidine Clinical Syndromes: Overdose/Toxicity

##### Signs and Symptoms:

- Bradycardia (often 40-55/min), Hypotension, Significant Sedation (often lasting 4-6+ hours)

##### Monitoring:

- Closely monitor airway, breathing, blood pressure, heart rate, and pulse oximetry.

##### Treatment:

- Naloxone to reverse the opioid/fentanyl-related respiratory depression.
  - ◊ Breathing and pulse oximetry typically improve, but sedation & bradycardia continue.
- Typically, supportive care, including airway/vital sign monitoring, and IV fluids if needed.
- Vasopressors, atropine, or transcutaneous pacing are typically not necessary.
- Sedation and bradycardia typically begin to improve in 4-6 hours.



DELAWARE DEPARTMENT OF HEALTH AND SOCIAL SERVICES  
DIVISION OF SUBSTANCE ABUSE AND MENTAL HEALTH

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Approved: 20 February 2026

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#### Medetomidine Clinical Syndromes: Withdrawal

##### Important to note:

- Medetomidine withdrawal syndrome starts earlier than opioid withdrawal.
- After resolution of overdose/toxicity symptoms, medetomidine withdrawal may rapidly worsen within hours.
- Complications of severe medetomidine withdrawal include encephalopathy, myocardial injury, acute kidney injury, and vomiting-related aspiration or esophageal injury.

##### Signs/Symptoms:

- Hypertension (often in the 180-200+ systolic range)
- Shaking/tremor (severe, can be confused for seizure)
- Tachycardia (often 130+/min)
- Decreased verbal response and catatonic-appearance

##### Monitoring:

- Closely monitor airway, breathing, blood pressure, heart rate, and pulse oximetry.
- Evaluate for signs of complications or end-organ damage due to severe withdrawal.

##### Treatment Guidance:

- General suggestions for treatment below are based on published data and regional expert opinion.
- These suggestions may be considered in producing facility-specific policies or protocols.
- Patient care must include an individualized assessment and plan based on patient-specific risks, allergies, and potential medication interactions or contraindications.

#### In the Outpatient Setting

<b>Mild/Early Medetomidine Withdrawal and able to tolerate oral medications</b>	<b>Severe Medetomidine Withdrawal -or- Rapid worsening of symptoms</b>
<b><u>Treat Symptoms:</u></b> Nausea, vomiting, diarrhea, pain, anxiety, etc.	Call 911 or refer to the emergency department.
<b><u>Treat Medetomidine Withdrawal:</u></b> Alpha-2-agonists: <ul style="list-style-type: none"><li>• <b>Clonidine</b> 0.2-0.3 mg PO every 6-8 hours. Tapering off clonidine over at least 2 weeks is recommended for continued control of withdrawal symptoms.</li></ul> NOTE: Consider potential risks of clonidine treatment (such as hypotension or bradycardia), however, patients using medetomidine typically have high alpha-2-agonist tolerance. <ul style="list-style-type: none"><li>• <b>Tizanidine</b> 2-4 mg PO every 8 hours, as needed for muscle cramps/spasm associated with medetomidine withdrawal.</li></ul>	
<b><u>Treat Opioid Withdrawal:</u></b> Start Medications for Opioid Use Disorder (MOUD): Buprenorphine-Naloxone (Suboxone®), if possible, or refer to an opioid treatment program for methadone treatment.	



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#### In the Emergency Department

<b>Mild/Early Medetomidine Withdrawal and able to tolerate oral medications</b>	<b>Severe Medetomidine Withdrawal and <u>unable</u> to tolerate oral medications</b>
<p><b><u>Treat Symptoms:</u></b> Nausea, vomiting, diarrhea, pain, anxiety, etc.</p>	<p>Treatments from “Mild/Early” plus, If continued severe signs/symptoms, such as hypertension, tachycardia, shaking/tremor, and intractable vomiting, THEN:</p>
<p><b><u>Treat Medetomidine Withdrawal:</u></b> Alpha-2-agonists:</p> <ul style="list-style-type: none"><li>• <b>Clonidine</b> 0.3-0.6 mg PO every 6-8 hours.</li><li>• <b>Clonidine</b> transdermal patch 0.3-0.6 mg/24h patch every week.</li></ul> <p>NOTE: Oral clonidine and transdermal clonidine patch <i>may be used together</i> as transdermal patch has prolonged onset of action (48+hours). Some facilities recommend higher oral clonidine doses or alternative alpha-2-agonist medications (such as guanfacine).</p> <ul style="list-style-type: none"><li>• <b>Tizanidine</b> 4 mg PO every 6-8 hours, as needed for muscle cramps/spasm associated with medetomidine withdrawal.</li></ul>	<p><b><u>Treat Medetomidine Withdrawal:</u></b> Start <b>Dexmedetomidine (Precedex)</b> infusion:</p> <ul style="list-style-type: none"><li>• Recommended higher starting dose of at least 0.5 mcg/kg/hr, with rapid titration.</li><li>• Consider loading dose of 0.5-1 mcg/kg over 20-30 minutes for <u>severe</u> withdrawal.</li><li>• Monitor per facility-specific policy (such as RASS and COWS scoring)<ul style="list-style-type: none"><li>◊ RASS of 0 is typically recommended for titration of dexmedetomidine.</li></ul></li><li>• Typical maximum dose is 1.5 mcg/kg/hr, however, there is some evidence for higher doses (facility and level-of-care dependent).</li><li>• Continuous telemetry monitoring.</li></ul>
<p><b><u>Treat Opioid Withdrawal:</u></b></p> <ul style="list-style-type: none"><li>• Start Medications for Opioid Use Disorder (MOUD): Buprenorphine-Naloxone (Suboxone®) or methadone, if possible.</li><li>• Opioid agonists (such as oxycodone or hydromorphone) are NOT indicated in the treatment of mild symptoms.</li></ul>	<p><b><u>Treat Opioid Withdrawal:</u></b></p> <ul style="list-style-type: none"><li>• Start Medications for Opioid Use Disorder (MOUD): Buprenorphine-Naloxone (Suboxone®) or methadone, if possible.</li><li>• Patients with combined severe opioid withdrawal and medetomidine withdrawal often need full opioid agonists to help control symptoms. Consider hydromorphone 2-4 mg IV and evaluate response.</li></ul>



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#### In the Hospital

Ongoing Inpatient Care	Discharge Planning Care
<p><b>Initially, continue care from “In the Emergency Department” section</b></p> <ul style="list-style-type: none"><li>• Level of care based on facility-specific policy. Some health systems have developed successful policies for stepdown/intermediate level of care if adequate monitoring is available.</li><li>• Continuous telemetry monitoring .</li><li>• Monitor per facility-specific policy (such as RASS and COWS scoring)<ul style="list-style-type: none"><li>◊ RASS of 0 is typically recommended for titration of dexmedetomidine.</li></ul></li></ul> <p><b>Dexmedetomidine (Precedex) infusion weaning:</b></p> <ul style="list-style-type: none"><li>• Should be slowly weaned. Recommendations include maintaining RASS of 0 during weaning.</li><li>• Goal of introducing oral alpha-2-agonists when able to tolerate PO medications.</li><li>• Continue clonidine transdermal patch.</li></ul>	<p><b>Focus on starting MOUD and arranging post-hospitalization plan for ongoing care</b></p> <ul style="list-style-type: none"><li>• Continue alpha-2-agonist (such as clonidine) after discharge from the hospital to prevent return of withdrawal symptoms.</li><li>• Alpha-2-agonist (clonidine) should be tapered over at least 2 weeks after discharge.</li><li>• Example post-hospitalization clonidine taper:<ul style="list-style-type: none"><li>◊ Days 1–5: Clonidine 0.2 mg q8h</li><li>◊ Days 6–10: Clonidine 0.1 mg q8h</li><li>◊ Days 11–14: Clonidine 0.1 mg q12h, then stop</li></ul></li></ul>
<p><b>Treat Opioid Withdrawal:</b></p> <ul style="list-style-type: none"><li>• Start Medications for Opioid Use Disorder (MOUD): Buprenorphine-Naloxone (Suboxone®) or methadone, if possible.</li><li>• Opioid agonists (such as oxycodone or hydromorphone) are NOT first-line in the treatment of mild opioid withdrawal.</li></ul>	<p><b>Treat Opioid Withdrawal:</b></p> <ul style="list-style-type: none"><li>• Continue MOUD (buprenorphine or methadone) after hospitalization and direct linkage to ongoing OUD care.</li></ul>

Additional specific clinical questions, please contact: [OEMS@delaware.gov](mailto:OEMS@delaware.gov)

