



NC DEPARTMENT OF  
**HEALTH AND  
HUMAN SERVICES**

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To: North Carolina Clinicians  
From: Kimberly McDonald MD, MPH, Section Chief, Chronic Disease and Injury

Re: Emerging Substances in Illicit Drug Supply

**Background**

North Carolina clinicians should be aware of the increasing detection of medetomidine, a potent veterinary sedative, and cyclophosphamide, a highly potent synthetic opioid, in the illicit opioid supply. Both substances have recently been identified in fentanyl and polysubstance drug samples across the United States, including reports in North Carolina.

Medetomidine is an alpha-2 agonist in the same drug class as xylazine but is substantially more potent. It is not approved for human use, however, its dextro-isomer, dexmedetomidine (Precedex®), is approved for procedural sedation in children and adults. Medetomidine was first identified in the United States illicit drug supply as early as 2021, with a growing number of detections reported among states since 2024. It is characterized by profound withdrawal symptoms often requiring ICU admission due to severe cardiovascular instability, as well as intoxication effects that include deep sedation and hallucinations.

Cyclophosphamide is a novel synthetic opioid belonging to a class of compounds called “orphines”, structurally related to fentanyl and other benzimidazoles. Although statewide prevalence data in North Carolina remain limited, clinicians should anticipate increasing exposure among patients who use the unregulated drug supply. Emerging reports suggest it may be significantly more potent than fentanyl, however, available information indicates that naloxone remains effective.

**Clinical Effects**

**Medetomidine**

Medetomidine produces central nervous system depression through alpha-2 adrenergic receptor agonism and may also cause:

- Prolonged sedation or unconsciousness
- Respiratory depression
- Bradycardia

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- Hypotension
- Hypothermia
- Altered mental status

Individuals exposed to medetomidine may present with sedation or decreased level of consciousness, which will not respond to naloxone. Since fentanyl co-exposure is common, naloxone should still be administered in all suspected overdoses because it will reverse respiratory depression and prevent overdose fatality. However, clinicians should recognize that naloxone will not reverse the sedative effects of medetomidine itself and repeated naloxone doses are generally not needed once adequate breathing has been restored. The goal of opioid overdose response is restoration of respirations, not necessarily restoration of consciousness.

Unlike xylazine, medetomidine does not appear to be associated with wound development.

Reports indicate that medetomidine withdrawal can be **life-threatening and may require hospitalization, frequently at the ICU level**, due to severe cardiovascular instability. Symptoms may begin within 4–6 hours of last use in regular users and typically peak between 18–36 hours. Symptoms of withdrawal may include:

- Severe hypertension, hypertensive emergency
- Sinus tachycardia (>100 beats per minute)
- Extreme agitation
- Anxiety, diaphoresis, tremor
- Severe nausea/vomiting resulting in inability to tolerate oral medications
- Hallucinations

Withdrawal management may require alpha-2 agonists such as clonidine or intravenous dexmedetomidine, which necessitates ICU-level monitoring, in addition to opioid agonist therapy (with methadone or buprenorphine) and supportive care for agitation as needed.

### **Cychlorphine**

Cychlorphine is a potent synthetic opioid that may cause:

- Severe respiratory depression
- Profound sedation or unconsciousness
- Constricted pupils
- Bradycardia
- Cyanosis or hypoxia

Standard overdose response measures remain essential, including naloxone administration, airway support, and extended monitoring.

### **Clinical Considerations**

Clinicians are encouraged to:

- Maintain a low threshold for hospital admission for patients with suspected medetomidine withdrawal, particularly those with hemodynamic instability or inability to tolerate oral medications.
- Continue standard opioid overdose response, including naloxone administration, respiratory support, and calling 911 if outside a hospital setting.
- Expect prolonged sedation and recognize that titrated naloxone dosing may be required.
- Monitor for cardiovascular instability, especially bradycardia and hypotension.
- Consider co-exposure to xylazine, medetomidine, or other sedating adulterants.
- Provide linkage to treatment providers for medications for opioid use disorder (MOUD), syringe services programs, and harm reduction resources.
- Encourage use of drug testing programs and/or test strips that are available for substances including fentanyl, xylazine, and medetomidine.

### **Public Health Implications**

Despite continued decline in drug overdose deaths nationally and in North Carolina, the illicit drug supply remains highly unpredictable. The emergence of substances including medetomidine and cychlorphine reflects the continued evolution of the drug supply. Similar to xylazine, many individuals exposed to these substances may be unaware they are present in the drugs they are using. Increased awareness among clinicians, emergency medical services, hospitals, and treatment providers will be important to overdose response, identifying and treating withdrawal symptoms, and reducing morbidity and mortality associated with exposure to emerging adulterants.

Identifying these substances may require testing the drug supply. Medetomidine's rapid metabolism may preclude clinically relevant testing of body fluids. Orphine testing is unavailable in the vast majority of clinical settings. Healthcare workers may need to identify individuals affected by these substances based on symptoms.

### **Additional Resources**

- [UNC Street Drug Analysis Lab](#)
- [CDC Medetomidine Situation Summary](#)
- [CDC Health Alert Network](#)
- [Philadelphia Department of Public Health Medetomidine Withdrawal Guidance](#)
- [North Carolina Safer Syringe Initiative](#)
- [Presentation and Management of Acute Medetomidine Withdrawal. American Journal of Health-System Pharmacy: AJHP : Official Journal of the American Society of Health-System Pharmacists. 2026. Zimmerman DE, Goodstein D, Durney PA, Patel-Francis SH, London KS.](#)
- [Emergence of Medetomidine in the Illicit Drug Supply: Implications for Emergency Care and Withdrawal Management. Annals of Emergency Medicine. 2026. Lynch MJ, Pizon AF, Yealy DM.](#)