

Naloxone Reverses the Apnea. It Does Not Reverse the Medetomidine.

Clinical Scenario

Your patient arrives unresponsive after a suspected opioid overdose. You give naloxone. Breathing resumes — but the patient remains deeply obtunded. More naloxone. No change.

The Pearl

Medetomidine is an alpha-2 adrenergic agonist now adulterating the illicit fentanyl supply at rapidly increasing rates. The DEA reports it is **200 to 300 times more potent than xylazine** and it is not an opioid. Naloxone works by blocking opioid receptors; it cannot touch a receptor pathway it was never designed to address.

When fentanyl and medetomidine are both present, naloxone reverses the opioid-driven apnea. The patient starts breathing. But the medetomidine-driven sedation persists through a completely separate mechanism. **There is no FDA-approved reversal agent for medetomidine in humans.**

Why It Matters

NFLIS medetomidine reports jumped from 247 (2023) to 2,616 (2024) to **8,233 in 2025** — detected in over a third of opioid-positive samples at 10 of 20 national surveillance sites. A patient who resumes breathing after naloxone but remains unresponsive may have medetomidine on board. Do not assume reversal is complete.

Medetomidine withdrawal resembles severe clonidine rebound — hypertension, anxiety, diaphoresis, fluctuating consciousness — and can require ICU-level care. Maintain the airway, support the patient, and communicate to the receiving team that a non-opioid adulterant is suspected.

Bottom Line: Naloxone reverses opioid-driven respiratory depression. It does not reverse medetomidine sedation. A patient who resumes breathing but remains obtunded after adequate naloxone dosing may have medetomidine on board. Treat the airway, support the patient, and do not wait for a reversal agent that does not yet exist.

References

1. Drug Enforcement Administration. Public Safety Advisory: Fentanyl Mixed with Xylazine, Medetomidine, Nitazenes, and Cychlorphine. DEA.gov. May 12, 2026.
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3. Capiod T, et al. Alpha-2 adrenergic agonists: pharmacology and clinical use. *Pharmacol Ther.* 2020;205:107424.

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