



Xylazine, Nitazenes, and the Changing Street Drug Landscape: What Pain Physicians Should Know

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Introduction

Patients in acute and chronic pain may often resort to self-medicating using illicit opioids, sometimes combined with other substances when bought from unregulated street suppliers. The street drug supply is increasingly contaminated with potent synthetic agents that complicate clinical care, becoming more frequent and complex each year. Xylazine, nitazenes, medetomidine, and related compounds are now common in heroin, fentanyl, stimulants, and counterfeit pills (labeled as one substance but actually containing different substances). These contaminated or counterfeit substances carry unique risks, including refractory overdoses, complex withdrawal syndromes, and physiologic instability that defies typical reversal strategies. For interventional pain physicians, this has immediate and critical implications. Contaminant exposure can blunt sedation responses, mimic infection or withdrawal, and elevate procedural risks. This review highlights the most clinically relevant adulterants (including newer compounds like nitazenes and medetomidine) and examines regional patterns to help guide risk assessment and care planning.

Methods

A targeted narrative literature review was conducted using PubMed, Scopus, and Web of Science to identify peer-reviewed studies, surveillance data, and toxicology reports related to emerging street drug contaminants with relevance to pain medicine. Search terms included combinations of “xylazine,” “nitazene,” “isotonitazene,” “metonitazene,” “medetomidine,” “brorphine,” “adulterant,” “synthetic opioid,” “fentanyl,” “veterinary sedative,” and “polysubstance.” Filters were applied to include English-language studies published between 2010 and 2025 involving human or forensic data. Titles and abstracts were screened for relevance to pharmacologic mechanisms, clinical presentation, or procedural implications for pain physicians. Reference lists of key publications were reviewed manually to identify additional sources. Public health surveillance data from agencies such as the CDC, DEA, and NIDA were also reviewed to characterize geographic patterns and temporal trends in contaminant emergence.

Contaminants, MOA, Clinical Effects, Impact for Pain Physicians

CONTAMINANT(S)	MECHANISM(S) OF ACTION	CLINICAL PRESENTATIONS	INTERESTING FACTS/STATISTICS	IMPLICATIONS FOR PAIN PHYSICIANS
Xylazine	α ₂ -adrenergic agonist (veterinary sedative)	Sedation, bradycardia, hypotension, respiratory depression, necrotic skin ulcers, refractory to naloxone	Found in >90% of Philadelphia opioid samples by 2021; now detected in ≥43 states (highest in VT and CT, ~9–10 deaths/100k)	Blunted sedation responses, hypotension during procedures, and necrotic wounds that may mimic infection; naloxone-resistant overdoses require supportive care
Nitazenes (isotonitazene, metonitazene)	Synthetic μ-opioid receptor agonists (ultrapotent opioids)	Profound respiratory depression, miosis, CNS depression, refractory overdose	Up to 1000× potency of morphine; increasingly found in counterfeit “fentanyl” tablets	Require multiple naloxone doses; unpredictable potency complicates peri-procedural opioid titration and post-procedure recovery
Medetomidine	α ₂ -adrenergic agonist (veterinary sedative)	Early hypertension → hypotension, bradycardia, deep sedation, prolonged recovery	First detected in Missouri/Colorado (2022); spread to Pennsylvania and Illinois	Causes hemodynamic instability and sedation variability; no reversal agent; consider enhanced monitoring and toxicology consults
Brorphine	Potent synthetic μ-opioid receptor agonist	Marked respiratory depression, CNS suppression, high overdose fatality risk	Emerged 2019; analogues variably detected	Potency similar to fentanyl; naloxone often effective but requires high cumulative dosing
Detomidine / Acepromazine	α ₂ -agonist / phenothiazine tranquilizer	Hypotension, bradycardia, variable sedation; prolonged CNS depression	Sporadic reports; limited human data	May mimic or compound opioid sedation; unpredictable responses during moderate/deep sedation
Polysubstance Combinations (fentanyl + xylazine ± stimulants)	Mixed opioid and adrenergic activity	Biphasic BP response, respiratory depression, necrotic ulcers, agitation → coma	>30% of fentanyl deaths in East involve cocaine; >50% in West involve methamphetamine	Alters sedation depth, vital stability, and analgesic response; regional trend awareness essential for pre-procedure risk assessment

Conclusion

Emerging contaminants like xylazine, nitazenes, and medetomidine have fundamentally changed the risks associated with illicit opioid use. Polysubstance exposure is now common, and many of these agents are resistant to standard reversal methods. For pain physicians, staying current on regional drug trends and associated clinical clues is essential. These exposures can alter sedation responses, increase periprocedural risks, and mislead diagnosis or treatment plans. Anticipating these variables can help improve procedural safety and patient outcomes.

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November 13-15, 2025 | Austin, TX

