

The Alpha Adulterants: Xylazine and Medetomidine in the Illicit Drug Supply

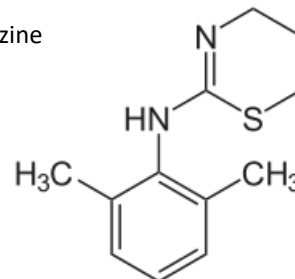
Xylazine and medetomidine are alpha-2 adrenergic receptor agonists that are increasingly found as adulterants in the US illicit drug market. Xylazine was first discovered in the early 2000s as an adulterant in Puerto Rico. The National Forensic Laboratory Information System (NFLIS) reported identifying 77,651 xylazine detections in drug reports between 1999 and 2024, with the number increasing from 2 cases in 1999 to 25,047 cases in 2024. The past four years (2021-2024) account for 90.5% of all xylazine exposures, and 41.2% of these cases are reported in the Northeast. Leading co-reported substances with xylazine included fentanyl (52.9%), heroin (10.26%), para-fluorofentanyl (6.38%), 4-ANPP (5.56%), and cocaine (4.02%). From 2021 through 2024, there were 2,796 reports of medetomidine in NFLIS drug reports- rising from 12 cases in 2021 to 2,276 reports in 2024, with 58.6% of these reports located in the Northeast. Medetomidine was co-reported with fentanyl (71.40%), xylazine (27.46%), heroin (5.49%), para-fluorofentanyl (5.18%) (Zhu *et al.*, 2025).

Xylazine, also known as “tranq”, was originally developed in 1962 as an antihypertensive agent, but human trials were halted due to central nervous system depressant effects, and was subsequently approved as a veterinary sedative to be used in animals. It is structurally similar to clonidine, phenothiazines, and imidazolines. Xylazine directly stimulates peripheral α -adrenoreceptors and stimulates presynaptic α_2 receptors, which modulate norepinephrine release. Xylazine also enhances vagal and baroreceptor activity (Greene *et al.*, 1988) and is associated with severe sedation, bradycardia, hypotension, and necrotic skin wounds (Perrone *et al.*, 2024). Tissue injury begins with small blisters/bumps and then progresses to necrotic skin ulcerations that affect large areas of skin, fat, and muscle, and in severe cases, necrosis penetrating tendons and bones. The mechanism remains unknown, although a possible hypothesis is that vascular insufficiency from acidic drugs and poor tissue perfusion from vasoconstriction lead to soft tissue injuries (Ciccarone *et al.*, 2025). Antibiotic treatment should be initiated in consultation with infectious disease consultants. However, these wounds are often not infected, and antibiotics should be considered with caution to prevent the development of resistance and complications. Wound care specialists should be consulted to support wound healing and management.

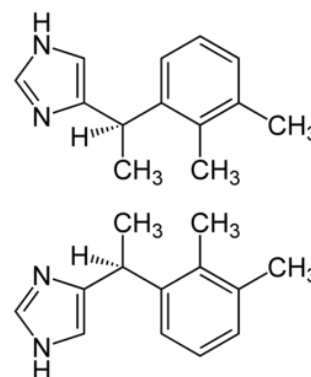
Medetomidine is referred to as “rhino tranq” or “mede,” and is a racemic mixture of dexmedetomidine and levomedetomidine, FDA approved in 1996 for IM and IV use only in dogs in the United States. Medetomidine exhibits a higher affinity for α_2 -adrenergic receptors than xylazine, resulting in greater potency and a longer duration of sedation (Virtanen *et al.*, 1988). Unlike xylazine, skin necrosis has not been reported with medetomidine alone.

Xylazine and medetomidine are commonly found in opioids like fentanyl; therefore, naloxone administration for respiratory support remains essential. Withdrawal management includes clonidine and a dexmedetomidine slow taper up to effect. When combined with fentanyl or heroin, the sedative effect is enhanced. Studies have shown that the administration of medetomidine in combination in dogs results in a significantly depressed respiratory rate compared to medetomidine alone. Opioids in combination have produced greater respiratory depression, acidosis, and hypoxemia. A multicenter randomized control trial in 1997 that compared the sedative and analgesic effects of medetomidine and xylazine in dogs demonstrated that the medetomidine group had consistently lower heart rates and sedation in comparison to the xylazine group (Tyner *et al.*, 1997), which is consistent with case reports in Philadelphia where patients presented with bradycardia of 30-40 beats/min with majority resolving within 10 hours (Murphy *et al.*, 2025).

Xylazine



Medetomidine



Did you know?

Atipamezole is a highly selective α_2 -adrenergic antagonist indicated for the reversal of the sedative and analgesic effects of medetomidine and dexmedetomidine approved for veterinary use; it is not available for human use.

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The University of Pittsburgh medical toxicology service evaluated 23 patients who experienced severe autonomic hyperactivity from the abrupt cessation of illegal opioids. Reported symptoms included nausea, vomiting, tremors, and autonomic hyperactivity. These patients were treated with dexmedetomidine or oral and transdermal clonidine and guanfacine in addition to phenobarbital (*Ostrowski et.al, 2025*).

There are currently no approved antidotes, and drug screens (serum and urine tests) are not widely available. Supportive care is essential, including supplemental oxygen, airway management, and vasopressors. For symptoms of bradycardia or hypotension, atropine, cardiac pacing, norepinephrine, or dopamine are recommended.

A priority should be placed on management of withdrawal: buprenorphine or methadone, in addition to clonidine and/or tizanidine, can be used. The Maryland Poison Center recommends clonidine 0.1-0.2 mg three times a day and/or tizanidine 2-4 mg three to four times a day for mild to moderate withdrawal symptoms. For refractory cases of withdrawal, dexmedetomidine can be titrated to a maximum dose of 1.5 mcg/kg/hr.

For symptomatic relief, benzodiazepines can be added to manage anxiety, agitation, and tremors. Close supervision is crucial; monitor for respiratory depression, hypotension, and bradycardia.

Management is complex and requires collaboration between different interdisciplinary teams. For guidance, please contact your local poison center at 1-800-222-1222.