

Information for providers

April 2023

What is xylazine?

Xylazine is a veterinary agent, approved in 1972, which is used for sedation, muscle relaxation and analgesia. In veterinary medicine, xylazine can be administered subcutaneously, intramuscularly, or intravenously.

Federal Guidance

The White House, Food and Drug Administration and The Drug Enforcement Agency have all released alerts to inform the general public and health care providers of the risk and presence of xylazine. Please see the alerts to the right for more information.

How does xylazine work?

Xylazine is a central α -2 adrenergic receptor agonist and is structurally similar to clonidine and dexmedetomidine (Precedex). Xylazine acts by decreasing the release of norepinephrine and dopamine with resultant sedation, muscle relaxation, and analgesia.

Is xylazine used in humans?

It is not approved for human use. In fact, human trials were discontinued due to adverse effects.

Why do physicians and other healthcare officials need to know about xylazine?

Xylazine is increasingly being found as an adulterant in the illicit drug supply and has been identified as one of the substances present in some fatal overdoses. It is most commonly found in combination with illicit opioids, such as heroin and fentanyl. However, it has also been found in combination with cocaine and psychostimulants (e.g., methamphetamine) and benzodiazepines. Many people who are using drugs adulterated with xylazine are not seeking it out and are unaware that it has been cut into the drugs they are buying.

Is xylazine detectable in toxicology screens?

Xylazine is not detected in routine toxicology screens, which are immunoassays. Currently, more advanced toxicology testing, such as chromatography, is required to detect xylazine. However, xylazine has a half-life of about 30 minutes and is rapidly eliminated from the body, which means even with the appropriate testing, it might be missed.

IDOH's toxicology program does test for the presence of xylazine when testing specimens from drug overdose death incidents.

Alerts

- [FDA Dear Colleague Letter](#)
- [FDA alert to Health Care Providers](#)
- [DEA Public Safety alert](#)
- [White House: Emerging Threat](#)

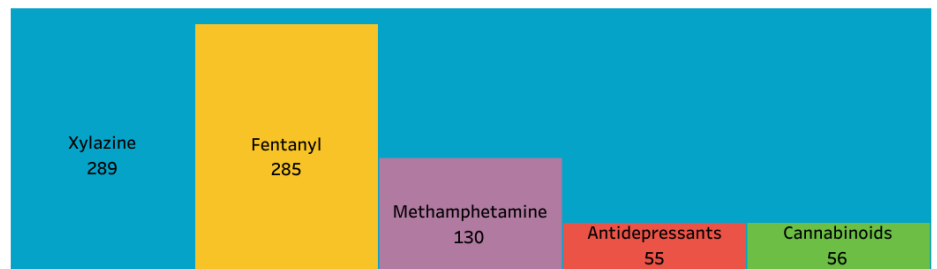
Xylazine in Indiana

Xylazine is one of the drugs tested for in overdose death incidents by IDOH’s toxicology vendor. From January 1, 2020 to April 11, 2023, there were 322 cases that were positive for xylazine; 120 positive results coming in each 2021 and 2020. This is over a 155% increase from 2019.

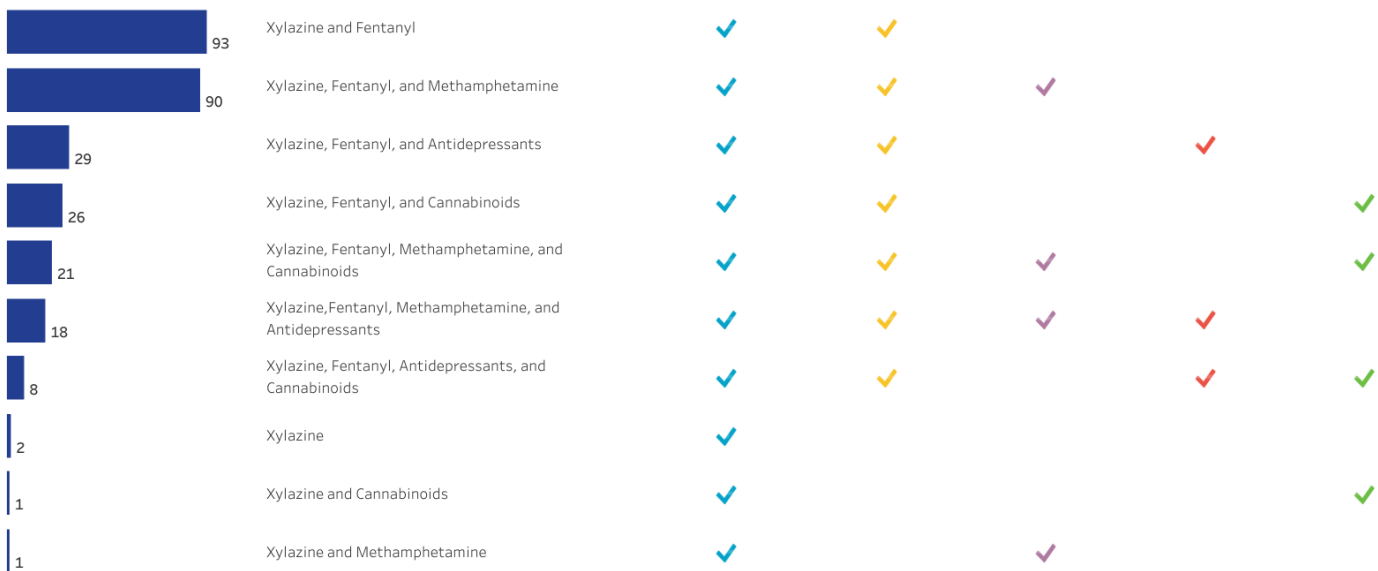
Prior to April 2023, xylazine was not appearing in ED ESSENCE data, but there has since been at least one identification of the drug in an overdose event.

Occurrence of Xylazine in 2020 to 2022 Decedents

Toxicology results are shown from 289 decedents who tested positive for xylazine and had a date of death between Jan. 1, 2020, and Dec. 31, 2022. Other drugs found in testing with xylazine: **fentanyl**, **methamphetamine**, **antidepressants** and **cannabinoids**.



Decedents who tested positive for:

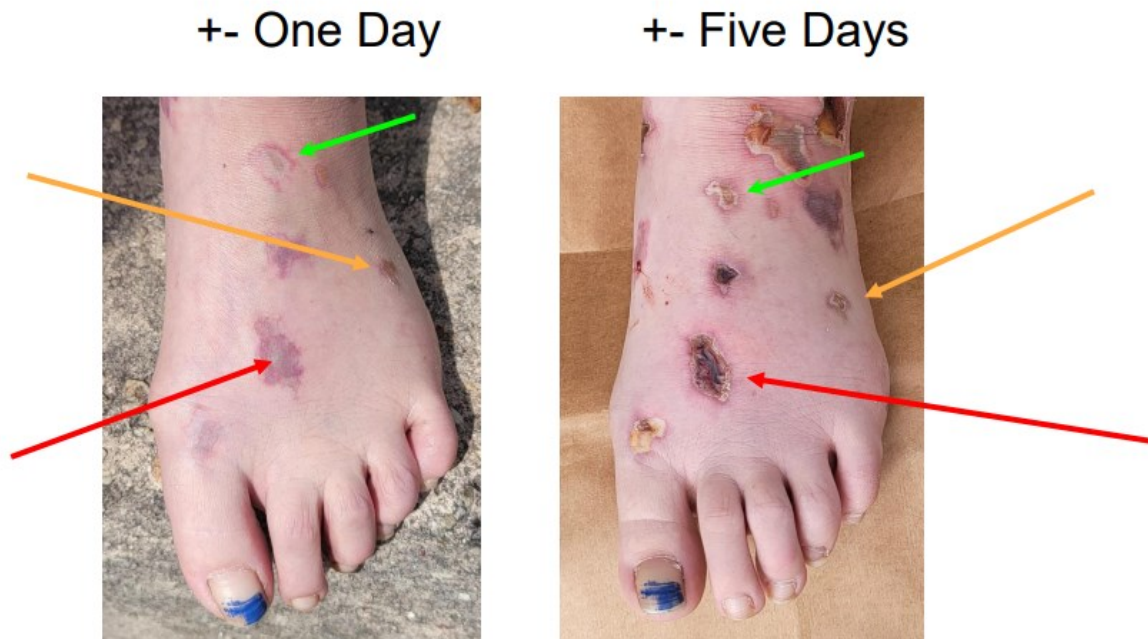


What are the clinical effects of xylazine use in humans?

- Hypotension (↓ blood pressure)
- Bradycardia (↓ heart rate)
- Arrhythmias
- Hyperglycemia
- Skin lesions and necrotic ulceration that are distinctly different from other soft-tissue infections and have been associated with risk for amputation
- Altered level of consciousness: drowsiness, coma
- Death

Xylazine-associated wounds

Xylazine has been associated with the development of skin ulceration. These ulcerations are often severe, presenting with necrosis and black eschars. While most commonly seen in persons who inject substances containing xylazine, the lesions may develop in areas distant from the injection site and in some instances occur in persons who have histories of smoking or snorting drugs but deny history of injection drug use. Again, because of limitations in testing for xylazine, the association with xylazine and the presence of these wounds is often presumptive and not confirmed by toxicology.



Orange arrow identifies non injection wound - distal from injection site.

Green and Red arrows point to the two different presentations of xylazine wounds.

Green arrow points to white centered (blanched) wound with red irregular edges.

Red arrow points to blistered skin with purple wound bed with irregular edges.

Care for xylazine-associated wounds typically requires debridement, long-term dressings [durable dressings], and an individualized follow-up plan based on access to clean water, housing status, access to medical supplies, comfort accessing healthcare, and comfort with self-care.

Xylazine and opioids

Xylazine can have effects that are synergistic with opioids. Such as, bradycardia, hypotension, sedation. Thus, xylazine in combination with opioids may increase the risk of sedation and potentially increase the risk of overdose. Yet, because xylazine is not an opioid, its effects cannot be reversed with the opioid antagonist, naloxone (brand name: Narcan). However, naloxone should always be administered in cases of suspected overdose. Opioids are almost always present in cases of overdose in which xylazine is present and while naloxone will not reverse the effects of xylazine, it will reverse the effects of any opioids that are present and can still be lifesaving.

How should healthcare professionals treat an overdose in which xylazine is suspected?

As opioids are almost always present in cases of overdose in which xylazine is present, naloxone should be administered to reverse the effects of any opioids that may be present. Supportive care is otherwise recommended for the effects of xylazine intoxication. This may include cardiovascular support, respiratory support, and glucose management.

While no medication is FDA approved for xylazine withdrawal, the following approaches are being used:

Replacement therapy with alpha-2-adrenergic agonists

- Clonidine,
- Dexmedetomidine,
- Tizanidine
- Guanfacine

Symptom management:

- Pain: Consider employing a multi-modal pain management strategy utilizing a combination of short acting opioids, Ketamine, Gabapentin, and NSAIDs
- Insomnia: Trazodone, Quetiapine, Mirtazapine
- Anxiety: Hydroxyzine, Benzodiazepines (judiciously)

Treat opioid use disorder and opioid withdrawal:

- If a patient is on opioid agonist therapy, then split dosing can increase analgesic effect and improve pain control.
- If a patient is initiating buprenorphine maintenance, then starting with small doses of buprenorphine (2mg or less) allows for concurrent use of short acting opioids that can improve pain control.

What happens with chronic xylazine exposure?

Repetitive exposure to xylazine has the potential to result in physiologic dependence resulting in the presence of withdrawal symptoms in the setting of abrupt discontinuation. Potential withdrawal symptoms include: severe anxiety, autonomic instability (rebound hypertension , tachycardia) and agitation.

There is minimal research to guide management of withdrawal symptoms associated with xylazine. However, physicians have described using the strategies described in the question above to manage the range of associated symptoms.

For additional information on drug overdose:

<https://www.in.gov/health/overdose-prevention/>

