MISSISSIPPI STATE DEPARTMENT OF HEALTH

This is an official
MS Health Alert Network (MSHAN) – Health Alert

MESSAGE ID:	**MSHAN-20230523-00595-ALT (Health Alert)**
RECIPIENTS:	**All Physicians, Hospitals, ERs, ICPs, NPs, PAs, and Healthcare Providers – Statewide**
	Tuesday, May 23, 2023
SUBJECT:	**Increased Xylazine Illicit Drug Use in the US and Mississippi**

Dear Colleagues,

- The number of xylazine-positive overdose deaths and xylazine detections are increasing in the US. According to a Drug Enforcement Administration report (see DEA Report: "The Growing Threat of Xylazine and its Mixture with Illicit Drugs-October 2022") the number of xylazine positive fatal overdoses increased in the Southern US by more than 1,100% between 2020 and 2021. Per the DEA report, the South also saw a 193% increase in xylazine detection among illicit drugs tested during this same timeframe. Both represent the highest increases across all US regions.
- Although not routinely tested, xylazine has been identified as a contributing factor among the deaths of 19 Mississippians from January 2020 through June 2022. Polydrug combinations included xylazine with heroin, fentanyl, or prescription opioids. Xylazine involved deaths are defined as deaths with xylazine as the primary or secondary cause of death on the death certificate data.

Xylazine Background Information

- Xylazine, a veterinary anesthetic, is increasingly identified as an adulterant mixed with illicit drugs like fentanyl, heroin, and cocaine. When combined with opioids, xylazine may have synergistic effects which can increase the risk of overdose and death.
- Xylazine is a depressant with similar effects as opioids, making it difficult to determine whether an individual has used one or both substances. The use of xylazine and opioids together increases the risk of life-threatening overdose.
- Xylazine is an alpha-2 adrenergic receptor agonist (similar to clonidine) and causes sedation, muscle relaxation, and analgesia.
- Xylazine can be orally ingested; inhaled; smoked; snorted; or injected subcutaneously, intramuscularly, or intravenously.
- Common signs/symptoms include central nervous system depression (e.g., sedation, disorientation, loss of consciousness), respiratory depression, bradycardia, hypotension and sometimes transient hypertension, and hyperglycemia.
- Xylazine can also cause peripheral vasoconstriction leading to poor tissue perfusion, skin ulceration, and necrosis which can lead to complications of cellulitis, abscess, and osteomyelitis.
    - Necrosis may occur at an injection site or at other body locations if the drug is inhaled, smoked, or snorted; repeated use increases the risk of tissue necrosis.

Mississippi Healthcare Provider Recommendations

Clinical management considerations include the following:

- Providers should be aware of the potential for overdoses and adverse events related to xylazine. Data indicates there is an increasing likelihood that overdoses involve multiple agents, including opioids and xylazine.
- Routine toxicology screening tests do not detect xylazine, but providers can check with clinical reference laboratories to see if xylazine-specific testing is available. **Results likely will not be timely to inform immediate clinical care.**
- There is no antidote or reversal agent available for use in humans, and naloxone will likely be ineffective against isolated xylazine toxicity. However, naloxone should be administered for suspected opioid-related overdoses, especially overdose-related respiratory depression, and repeated naloxone administration may be necessary for highly potent opioid exposures.
- Inpatient management of xylazine withdrawal may benefit from use of Dexmedetomidine, Tizanidine, Clonidine, Guanfacine, Ketamine, Gabapentin, Pentobarbital, or Benzodiazepines (with caution). See the Pennsylvania Department of Public Health HAN.
- Supportive care is the mainstay of therapy for xylazine toxicity, including IV fluids, blood glucose monitoring, supplemental oxygen, airway management, blood pressure and cardiac monitoring and support.
- No medications have been FDA-approved to manage xylazine withdrawal symptoms. Case reports suggest that low-dose alpha-2 adrenergic agonist replacement therapy (e.g., clonidine, tizanidine, dexmedetomidine) may help withdrawal symptoms associated with sympathetic over-activity, including autonomic instability and cardiovascular dysregulation.
- Necrotic skin wounds or ulcerations should be evaluated for debridement and wound care. Patients may also need pain control for skin wounds – see the CDC's updated Clinical Practice Guideline for Prescribing Opioids for Pain.
- Treat a patient's underlying substance use disorder (SUD) and counsel patients about harm reduction techniques.
- Report suspected xylazine toxicity to the Mississippi Poison Control Center at 1-800-222-1222.
- Report Adverse Events related to xylazine to the FDA MedWatch Adverse Event Reporting Program

Resources:

- FDA Letter to healthcare providers about risks to patients exposed to xylazine.
- CDC: Updated Clinical Practice Guideline for Prescribing Opioids for Pain.
- The Growing Threat of Xylazine and its Mixture with Illicit Drugs (dea.gov)

- FDA Adverse Event Reporting FDA MedWatch Adverse Event Reporting Program
- CDC Xylazine FAQ What You Should Know About Xylazine | Drug Overdose | CDC Injury Center

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Alerting Message Specification Settings

Originating Agency:	Mississippi State Department of Health
Alerting Program:	**MS Health Alert Network (MS HAN)**
Message Identifier:	CDCHAN-20230523-00595-**ALT**
Program (HAN) Type:	**Health Alert**
Status (Type):	Actual ()
Message Type:	Message/Information
Reference:	MSHAN-00595
Severity:	Unknown
Acknowledgement:	No
Sensitive:	Not Sensitive
Message Expiration:	Undetermined
Urgency:	Undetermined
Delivery Time:	600 minutes

Definition of Alerting Vocabulary and Message Specification Settings

Originating Agency: A unique identifier for the agency originating the alert.

Alerting Program: The program sending the alert or engaging in alerts and communications using PHIN Communication and Alerting (PCA) as a vehicle for their delivery.

Message Identifier: A unique alert identifier that is generated upon alert activation (MSHAN-yyymmdd-hhmm-TTT **(ALT=Health Alert, ADV=Health Advisory, UPD=Health Update, MSG/INFO=Message/Info Service**).

Program (HAN) Type: Categories of Health Alert Messages**.**

Health Alert: Conveys the highest level of importance; warrants immediate action or attention.

Health Advisory: Provides important information for a specific incident or situation; may not require immediate action.

Health Update: Provides updated information regarding an incident or situation; unlikely to require immediate action.

Health Info Service: Provides Message / Notification of general public health information; unlikely to require immediate action.

Status (Type):

- Actual: Communication or alert refers to a live event
- Exercise: Designated recipients must respond to the communication or alert
- Test: Communication or alert is related to a technical, system test and should be disregarded

Message Type:

- Alert: Indicates an original Alert
- Update: Indicates prior alert has been Updated and/or superseded
- Cancel: Indicates prior alert has been cancelled

Reference: For a communication or alert with a Message Type of "Update" or "Cancel", this attribute contains the unique Message Identifier of the original communication or alert being updated or cancelled. "n/a" = Not Applicable.

Severity:

Extreme:	Extraordinary threat to life or property
Severe:	Significant threat to life or property
Moderate:	Possible threat to life or property
Minor:	Minimal threat to life or property
Unknown:	Unknown threat to life or property

Acknowledgement: Indicates whether an acknowledgement on the part of the recipient is required to confirm that the alert was received, and the timeframe in which a response is required (Yes or No).

Sensitive:

Sensitive:	Indicates the alert contains sensitive content
Not Sensitive:	Indicates non-sensitive content

Message Expiration: Undetermined.

Urgency: Undetermined. Responsive action should be taken immediately.

Delivery Time: Indicates the timeframe for delivery of the alert (15, 60, 1440, 4320 minutes (.25, 1, 24, 72 hours)).