# PENNSYLVANIA DEPARTMENT OF HEALTH
# 2024 – PAHAN – 763 – 08 – 1- ADV

## Emerging Substances in the Illicit Drug Supply

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| **DATE:** | August 1, 2024 |
| **TO:** | Health Alert Network |
| **FROM:** | Debra L. Bogen, M.D., FAAP, Secretary of Health |
| **SUBJECT:** | **Emerging Substances in the Illicit Drug Supply** |
| **DISTRIBUTION:** | Statewide |
| **LOCATION:** | Statewide |
| **STREET ADDRESS:** | N/A |
| **COUNTY:** | N/A |
| **MUNICIPALITY**: | N/A |
| **ZIP CODE:** | N/A |

**This transmission is a "Health Advisory" that provides important information for a specific incident or situation; may not require immediate action.**

**HOSPITALS:** PLEASE SHARE WITH ALL MEDICAL, PEDIATRIC, NURSING AND LABORATORY STAFF IN YOUR HOSPITAL**; EMS COUNCILS:** PLEASE DISTRIBUTE AS APPROPRIATE; **FQHCs:** PLEASE DISTRIBUTE AS APPROPRIATE **LOCAL HEALTH JURISDICTIONS**: PLEASE DISTRIBUTE AS APPROPRIATE; **PROFESSIONAL ORGANIZATIONS:** PLEASE DISTRIBUTE TO YOUR MEMBERSHIP; **LONG-TERM CARE FACILITIES:** PLEASE SHARE WITH ALL MEDICAL, INFECTION CONTROL, AND NURSING STAFF IN YOUR FACILITY


**Summary**

- There is an increasing number of emerging substances circulating in the illicit drug supply.
- If a person is suspected to have experienced a drug overdose, but the toxicology results are inconclusive or negative, it is possible an emerging substance could have contributed and testing for the drugs noted below is recommended if possible.
- Use naloxone to respond to any suspected overdose. Naloxone won't harm someone if they're overdosing on other drugs. Rescue breathing and/or oxygen administration may also be needed to respond to an overdose involving xylazine or other sedatives.
- If you have any questions, please call DOH at 1-877-PA-HEALTH (1-877-724-3258) or your local health department.
- For consultation related to potential exposures and/or overdoses, please contact the Poison Control Center at 1-800-222-1222.


## Background

This Health Alert Network (HAN) Update is to alert Pennsylvania's healthcare professionals, first responders, medical examiners and coroners to important new developments in the evolving drug overdose epidemic. As the drug overdose epidemic continues to evolve, so does the drug supply. Most overdoses continue to involve illicitly manufactured fentanyl. However, polysubstance use is increasingly common and most fatal overdoses involve more than one substance. The Pennsylvania

Department of Health (PADOH) continues to monitor the emergence of new and novel substances identified by toxicology reports collected from fatal drug overdose decedents.

## Emerging Substances

Through surveillance of toxicology reports of overdose decedents, the PADOH has become aware of several emerging substances contributing to overdoses across Pennsylvania, which include:

- **Designer Benzodiazepines**
- **Nitazenes**
- **Tianeptine**
- **Carfentanil**

**Designer benzodiazepines** are a broad class of drugs that could be structurally analogous to prescribed benzodiazepines, metabolites of prescribed benzodiazepines, or benzodiazepines that are not approved for use in the United States. Designer benzodiazepines amplify the risk of death when used with opioids. There have been a growing number of designer benzodiazepines in the drug supply, which have been increasingly found to contribute to drug overdose deaths in Pennsylvania. Designer benzodiazepines contributed to **59** overdose fatalities in Pennsylvania in 2022 and increased to **147** so far in 2023 (as of June 2024). In 2022 and 2023, bromazolam most commonly contributed to death, while etizolam was more likely to contribute to overdose death in previous years.

**Nitazenes** are a group of synthetic opioids that can be more potent than fentanyl and have been increasing in use since 2019. Nitazenes, including isotonitazene, protonitazene, metonitazene, N-pyrrolidino etonitazene, cause similar effects as opioids and are often found in the presence of other drugs. Nitazenes contributed to fewer than **6** overdose deaths in Pennsylvania in 2020 and 2021, and **15** drug overdose fatalities so far in 2023 (as of June 2024). Low counts in previous years may be due to nitazenes not yet being included in routine toxicology testing for overdose decedents. Additional information on nitazenes can be found here.

**Tianeptine** is an atypical tricyclic antidepressant and causes effects similar to opioids. Tianeptine is not approved for medical use by the United States Food and Drug Administration. However, tianeptine is sold online and at gas stations and presents as an emerging substance for misuse. Tianeptine contributed to less than **6** overdose fatalities in Pennsylvania in 2022 and 2023 (as of June 2023). Additional information on tianeptine can be found here.

**Carfentanil**, a synthetic opioid used by veterinarians to tranquilize large animals, contributed to a significant number of drug overdose deaths in previous years with more than **120** deaths in Pennsylvania related to carfentanil from 2017-2019. While Pennsylvania has seen a decrease in more recent years with fewer than **6** overdose deaths involving carfentanil between 2020 and 2023 (as of June 2024), Pennsylvania's neighboring state, Ohio, issued a warning on carfentanil reemergence in September 2023. Harm reduction and prevention recommendations are available in CDC's Health Alert Network update released July 11, 2018.

For more information on national trends in drugs involved in unintentional and undetermined drug overdose deaths, including nitazenes, designer benzodiazepines, and carfentanil, please visit CDC's State Unintentional Drug Overdose Reporting System dashboard.

## Recommendations

Currently most designer benzodiazepine, carfentanil, and nitazene overdose deaths also contained fentanyl and often xylazine and cocaine. The DEA reports that "drug cocktails," or samples containing more than one substance, are the new normal rather than the exception and these drug cocktails often include opioids. In response to the volatile drug supply, the PA DOH recommends the following:

1. **Use naloxone to respond to any suspected overdose.**
    - Naloxone should always be administered for all suspected overdoses as many of the drugs included in this HAN are opioids or are most often utilized in combination with opioids, such as fentanyl, and naloxone will reverse the effects of any opioids that are present.
    - As with xylazine, the extreme sedation that may be associated with designer benzodiazepines emphasizes the need for rescue breathing and/or oxygen administration. In addition to respiratory support, recommended supportive care includes glucose management and cardiovascular support.
    - Considerations on administering multiple doses of naloxone:
        i. If the person does not start breathing after 2-3 minutes (and after providing rescue breaths), administer an additional dose of naloxone and continue rescue breaths.
        ii. If there is still no response and additional doses are available, administer additional doses every 2-3 minutes and continue rescue breaths until emergency medical assistance arrives or the person begins breathing.
        iii. If the person stops breathing during recovery, give a second dose of naloxone immediately.
        iv. The goal is to get the person breathing on their own even if they do not wake up.
    - Tianeptine acts as a full mu-opioid receptor (MOR) and a weak delta-opioid receptor (DOR) agonist; as a full MOR agonist, high doses of tianeptine can also precipitate symptoms of respiratory depression, which can be potentially reversed with naloxone.

2. **Be prepared to manage opioid, xylazine, and/or benzodiazepine withdrawal symptoms in presenting patients.**
    - Withdrawal is a physiological response to the sudden quitting or slowing of use of a substance upon which the body has grown dependent. Withdrawal symptoms can be life-threatening.
    - Patients using illicit substances may not know if their substance contained designer benzodiazepines, xylazine, or synthetic opioids.
    - Please note that a person who has been revived may be uncomfortable and agitated. If they do not wish to participate in further healthcare services, naloxone and other harm reduction supplies should be provided to them for future use.
    - While little information is available in the literature about designer benzodiazepine dependence and withdrawal, it's been suggested that designer benzodiazepines may produce similar effects and withdrawal symptoms and may be more addictive and cause more severe withdrawal than prescription benzodiazepines. Treatment guidelines for prescription benzodiazepine withdrawal may be challenging to implement as there is not enough information to reliably convert designer benzodiazepine dosages to prescription benzodiazepine dosages.

Designer benzodiazepines, nitazenes, tianeptine, and carfentanil are emerging substances that may be found in combination with other common substances or may be implicated in overdoses when common substances are not found. Expanding the scope of toxicological testing and drug testing programs may aid in the detection of emerging substances circulating in the drug supply in Pennsylvania and help determine the most effective overdose intervention.

If you have any questions, please call DOH at 1-877-PA-HEALTH (1-877-724-3258) or your local health department.

**Additional Information**

- PA Groundhogs Drug Checking.
- Naloxone (pa.gov)
- PA Overdose Prevention Program (POPP): POPP offers multiple formulations of naloxone as well as drug checking strips designed to detect xylazine and fentanyl at no cost to organizations across Pennsylvania.
- PA DOH Interactive Data Reports
- DEA information on Nitazenes
- Tianeptine article
- Xylazine HAN
- Educational Modules for Implementing MOUD in Emergency Departments

**Individuals interested in receiving further PA-HANs are encouraged to register at** HAN Notification Registration (mir3.com)

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.

This information is current as of August 1, 2024 but may be modified in the future. We will continue to post updated information regarding the most common questions about this subject.