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Health Alert

Nitazene analogs, a novel class of synthetic opioids more potent than fentanyl, detected in Philadelphia
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SUMMARY POINTS

- Nitazene analogs are synthetic opioids that are up to 40 times more potent than fentanyl
- First identified in the United States in 2019
- First identified in Philadelphia as early as October 2022
- Individuals who experience an opioid overdose after using nitazene analogs will respond to naloxone (e.g., Narcan®).

What are nitazene analogs? Nitazene analogs are a novel class of synthetic opioids that can be up to 40 times more potent than fentanyl and up to 500 times more potent than morphine. Nitazene analogs vary in potency and include isotonitazene, metonitazene, and N-pyrrolidino etonitazene. The Drug Enforcement Administration has classified ten nitazene analogs as Schedule I drugs since there is no approved medical use for nitazene analogs in the United States, and initial pharmacologic evaluations do not support any medical or veterinary use.^{i,ii,iii} However, novel nitazene analogs that are not explicitly scheduled in the United States, such as N-desethyl isotonitazene, continue to be discovered through drug checking programs.

In December 2022, N-desethyl isotonitazene was the first nitazene analog to be detected in the Philadelphia drug supply among four unique samples suspected to be “dope” with the following stamps: “hearse”, “atco”, and “show and tell”. There are indications, however, that nitazene analogs were present in the drug supply as early as October 2022.

Where are nitazene analogs being used? In 2019, isotonitazene was the first nitazene analog found in the US and has since been identified in over 250 drug overdose deaths. In 2021, metonitazene and N-pyrrolidino etonitazene were each identified in over 100 drug overdose deaths. Nitazene analogs have been identified in many parts of the country, including the Midwest, South, Southwest, and East. Based on nationwide toxicology reports, it is estimated that there have been between 1,000 and 2,000 deaths associated with nitazene analogs across the entire US since 2019, although numbers are likely underestimated in the absence of routine testing for this class of drugs.^{iv}

What do nitazene analogs look like? Nitazene analogs can appear in a variety of colors and preparations, including yellow, brown, gray, or off-white powders, and are most often sold as “heroin” or “fentanyl” in illicit drug markets. Nitazene analogs are sold online as powders, ready-to-use nasal sprays, or counterfeit pills.

How are nitazenes used? Similar to fentanyl and heroin, nitazene analogs are most commonly used intravenously and intranasally via spray or insufflation, but can also be smoked, vaporized or taken sublingually.

What is the remedy for overdose involving nitazene analogs? Naloxone (e.g., Narcan®) is effective in treating people experiencing a nitazene-related opioid overdose.^v This medication is often used to revive people who have overdosed on opioids (e.g., heroin or fentanyl). Higher doses and/or redosing of naloxone may be needed based on clinical signs and symptoms. More research is needed to determine the optimal dose in treating nitazene analog overdoses, there is no evidence of naloxone-resistant new synthetic opioids.

What is the public health impact of nitazene analogs?

Since the onset of the opioid epidemic, novel synthetic opioids (NSOs) have been reported as the largest contributors to drug overdose deaths in the US, led primarily by fentanyl. However, a second tier of NSOs have emerged called the nitazene analogs, a subclass of opioids not used for medicinal purposes and that retain a high potential for overdose due to increased potency compared to fentanyl. Fentanyl test strips cannot detect nitazene analogs.

What is PDPH doing?

- Collaborating with the Center for Forensic Science Research & Education for surveillance of the drug supply in Philadelphia.
- Expanding the capacity of the Philadelphia Medical Examiner's Office to detect nitazene analogs.
- Distributing naloxone and providing training to individuals and organizations on how to respond to drug overdoses and administer naloxone.
- Partnering with [Next Distro](https://nextdistro.org/philly) to provide free naloxone to Philadelphians, regardless of insurance status. Visit nextdistro.org/philly to learn how use naloxone and receive a kit in the mail.
- Naloxone for all. Conducting [academic detailing](#) and outreach to healthcare providers to promote naloxone prescribing for all patients, not just those prescribed opioids.
- Pennsylvania has a standing order for naloxone, and it should be available at all pharmacies. Visit www.phillynaloxone.com for more information on how to get naloxone in Philadelphia.

ⁱ https://www.who.int/docs/default-source/controlled-substances/43rd-ecdd/isonitazene-43rd-final-complete-a.pdf?sfvrsn=c98d9c9_2

ⁱⁱ https://www.cfsre.org/images/content/reports/public_alerts/2019.11.20.Public-Alert_Isotonitazene_NPS-Discovery_111919-1.pdf

ⁱⁱⁱ https://www.npsdiscovery.org/wp-content/uploads/2021/01/Public-Alert_Metonitazene_NPS-Discovery_012521.pdf

^{iv} Barenholtz E, et al. Online surveillance of novel psychoactive substances (NPS): Monitoring Reddit discussions as a predictor of increased NPS-related exposures. International Journal of Drug Policy. 2021 Dec 1;98:103393.

^v https://www.cfsre.org/images/content/reports/public_alerts/2021.12.03.Public-Alert_Next-Generation-Opioids-in-Clinical-Cases_NPS-Discovery_120321.pdf