

Health Alert

In Philadelphia, novel synthetic opioids with wide-ranging potency have been detected in the illicit drug supply and among people who unintentionally overdosed.

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SUMMARY POINTS

- Carfentanil has been found in the illicit drug supply, and multiple nitazene analogs have been found in both the illicit drug supply and overdose decedents.
- Drug checking and blood samples with newly detected synthetic opioids also contained multiple sedating substances.
- All novel opioids detected are responsive to naloxone. People who use drugs containing these substances and experience an overdose will respond to naloxone. Additional actions such as rescue breathing and supplemental oxygen may support response efforts.

In response to identification of N-Desethyl Isonitazene in Philadelphia's drug checking services of "dope" (illicit heroin/fentanyl) in December of 2022, the Medical Examiner's Office partnered with the Division of Substance Use Prevention and Harm Reduction (SUPHR) to pilot enhanced nitazene surveillance among drug overdose decedents. To date, four distinct nitazene analogs (N-Pyrrolidino Etonitazene, N-Desethyl Isonitazene, metonitazene, and protonitazene) have been detected in decedent toxicology with potency ranging from equipotent to 20 times more potent than fentanyl. Concurrent drug checking has identified two higher potency nitazenes (N-Pyrrolidino Etonitazene and N-Desethyl Isonitazene) as well as carfentanil, a fentanyl analog 100 times more potent than fentanyl, in several samples from the illicit drug supply in Philadelphia.

Retrospective surveillance of overdose decedent toxicology from October to December 2022 identified 12 decedents had an indication of N-desethyl isonitazene, the same nitazene analog identified in SUPHR's drug checking services in December 2022. These individuals died of unintentional overdose in November to December 2022. Another two nitazene analogs, protonitazene (approximately four times more potent than fentanyl) and metonitazene (equipotent to fentanyl), were identified in an overdose decedent whose death occurred in June 2023.

Drug checking services have identified N-Pyrrolidino Etonitazene in seven samples of dope that were collected in October 2023 to February 2024. The samples also included fentanyl, xylazine, fentanyl precursors (4-ANPP and phenylethyl-4-ANPP). The Medical Examiner's Office identified the same nitazene analog (N-Pyrrolidino Etonitazene) in four people who have died of unintentional overdoses and two people with traumatic causes of death since December 2023 with results confirmed by the Center for Forensic Science, Research, and Education (CFSRE). All blood samples that contained this nitazene analog also contained xylazine and fentanyl. Four samples contained bromazolam, a novel benzodiazepine that increases risk of overdose when mixed with other sedating substances, such as opioids. Four samples contained cocaine, and two samples contained the fentanyl analog, para-Fluorofentanyl. It is not known if individuals who took these substances purchased them as "dope," as pressed pills, or in some other form. It is also not known if individuals with blood samples positive for cocaine and opioids intended to use these substances together.

Since December 2022,¹ four distinct nitazene analogs have been identified in overdose decedents in Philadelphia: N-Desethyl Isonitazene, Metonitazene, Protonitazene, and most recently N-Pyrrolidino Etonitazene. Codetected substances are shown in Table 1. N-Pyrrolidino Etonitazene is an opioid that has been identified in the United States since 2021 and is estimated to be about ten times more potent than fentanyl.²

A dope sample collected in January 2024 contained carfentanil. The sample with carfentanil tested positive for fentanyl, para-fluorofentanyl, xylazine, and 4-ANPP. Carfentanil is a synthetic opioid estimated to be 100 times more potent than fentanyl and has not been identified in Philadelphia since June 2017,³ when carfentanil was found in blood samples of two people who died of unintentional overdoses.

As more potent opioids, smaller amounts of dope can lead to unintentional overdose, especially among people with low opioid tolerance. It is important to note that to date, these novel substances have only been identified in ‘dope,’ though caution among persons who use any substances is critical to limit adverse events. Both nitazene analog and carfentanil overdoses can be reversed with naloxone (e.g., Narcan™, ReVive™), and rescue breathing may be necessary in instances in which someone also has ingested non-opioid sedatives like xylazine or benzodiazepines. Additional doses of naloxone doses may be necessary,⁴ and number of naloxone doses has not been shown to impact mortality among people who have overdosed.⁵ Nitazene test strips are not widely available. Due to smaller amounts typically present in these samples, fentanyl test strips may be unable to detect the presence of carfentanil,⁶ therefore education and access to naloxone is imperative.

For people with opioid use disorder, withdrawal from nitazene analogs and many novel synthetic opioids has not been characterized in the literature. Anecdotal experiences from people who use drugs in Philadelphia suggest that the onset of withdrawal from nitazene analogs occurs more quickly and with more severity. Providers treating people using illicit opioids should be aggressive with management of pain and withdrawal symptoms.

The illicit drug supply is ever-changing and increasingly dangerous. Novel synthetic opioids in Philadelphia have been first identified through drug checking, and increased drug checking can aid detection and response to emerging substances. Providers (doctors, nurses, social workers, case managers, and peer specialists) should talk to and listen to their patients about their substance use. Providers can discuss the volatility of the illicit drug supply, encourage safer use practices, and ask patients with substance use disorder and history of substance use about their openness to treatment.

Safer use practices can include:

- Testing their drugs with test strips, which have been decriminalized statewide in PA along with other drug testing devices ([Act 111](#))
- Carrying and knowing how to use naloxone
- Trying not to use alone, and if they are able and comfortable using around someone else making sure naloxone is available and the person can administer it
- Trying a smaller amount of their drug to see how it feels before using their normal dose
- Speaking with their community to see if certain drugs are causing adverse events for people who use substances and letting people know when they experience an adverse event

Table 1. Codetected substances* identified in drug checking services and decedent blood toxicology for samples with novel synthetic opioids (metonitazene, protonitazene, N-Pyrrolidino Etonitazene, N-Desethyl Isonitazene, and carfentanil).

	Opioids only, N (Row %)	Opioids and sedatives, N (Row %)	Opioids and stimulants, N (Row %)	Opioids, sedatives, and stimulants, N (Row %)
Drug Checking (n=13)	0 (0)	11 (84.6)	0 (0)	2 (15.4)
Decedent toxicology (n=20)	0 (0)	4 (20.0)	4 (20.0)	12 (60.0)

*Codetected opioids included fentanyl, para-fluorofentanyl, and methadone. Codetected sedatives included xylazine, bromazolam, flubromazepam, and diazepam. Codetected stimulants included cocaine, cocaethylene, amphetamine, and methamphetamine.

Resources

Substance Use Disorder Treatment

- Behavioral Health Services Initiative (uninsured): 1-215-546-1200
- Community Behavioral Health (Medicaid): 1-888-545-2600
- CareConnect Warmline: 484-278-1679
- SAMHSA National Helpline: 800-662-HELP (4357)

Recommend patients try not to use alone, and provide resources if that is what they are doing, such as:

- Never Use Alone: 877-696-1996
- The Brave App – free to download on app stores
- Canary App – free to download on app stores

Learn how to get and use naloxone – www.substanceusephilly.com

Get naloxone & fentanyl test strips for free and confidentially – <https://nextdistro.org/philly>

Learn how to use fentanyl test strips

- <https://www.cdc.gov/stopoverdose/fentanyl/fentanyl-test-strips.html>
- <https://www.youtube.com/watch?v=GmhE6UOZ9YY>

References

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