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Maryland Poison Center
UNIVERSITY OF MARYLAND SCHOOL OF PHARMACY

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The Maryland Poison Center's Monthly Update: News, Advances, Information

Nitazenes—the mu kids on the block

Nitazenes are synthetic opioids from the benzimidazole-opioid class of drugs. They do not resemble fentanyl in structure but nonetheless act as highly potent mu-opioid agonists and can be up to 40 times more potent than fentanyl. The Washington/Baltimore High Intensity Drug Trafficking Area (HIDTA) released a bulletin in April 2022 warning about isotonitazene in Maryland and Washington, DC. At the time of the bulletin, 17 cases had been identified in Maryland and 2 cases in Washington, DC. There have been about 2,400 reports of nitazene use in the United States since 2019 *('Benzimidazole-opioids', 2022)*. Isotonitazene was the predominant drug implicated in nitazene-related fatalities from March 2019 to July 2020. After isotonitazene scheduling in June 2020, metonitazene, which is approximately twice as potent as isotonitazene, became the predominant drug. Etonitazene, flunitazene, and butonitazene are emerging nitazenes that have been detected in 2021 *(Montanari et al., 2022)*.

Because they are mu-opioid agonists, nitazenes have effects similar to those of other mu-opioid agonists such as heroin and fentanyl, and overdose can cause respiratory depression. Importantly, nitazene overdose responds to naloxone/Narcan® administration, though additional doses of naloxone may be required due to their potency *(Nitazenes (CCENDU Drug Alert), 2022)*. A Morbidity and Mortality Weekly Report (MMWR) from Tennessee found that naloxone was only administered in 23% of nitazene-involved fatal overdoses, indicating there is increasing need for awareness of nitazenes and the use of naloxone in treating opioid overdoses among clinicians and first responders *(Roberts, 2022)*.

Drugs such as heroin and fentanyl may be cut with nitazenes. In Maryland, nitazenes have been found mixed with fentanyl, methamphetamine, diphenhydramine, and others (*NDEWS Weekly Briefing, Issue 106*, 2022). However, fentanyl test strips do not detect nitazenes, and nitazenes are not routinely tested for in urine drug screens, meaning it is difficult to identify and monitor for the presence of these drugs within the drug supply *(Nitazenes (CCENDU Drug Alert), 2022)*.

Nitazenes may appear as a yellow, brown, or off-white powder. Nitazenes have also been detected in counterfeit pills marked as "Dilaudid®" and "oxycodone" *(DEA - Nitazines, 2022)*. The most common route of nitazene administration is injection, though smoking, snorting, and ingestion are also possible.

In 2021, there were nearly 108,000 drug overdose deaths, with synthetic opioids involved in 75% of those deaths *(DEA - Nitazines, 2022)*. Due to their high potency, nitazenes have an increased potential for abuse and overdose, though overdoses do respond to naloxone administration. While rates of nitazene use remain low, this is an important emerging agent to be aware of, especially as testing for and detection of these agents remains limited. If you are seeing a patient with suspected/confirmed opioid poisoning, we recommend consulting your regional poison center at 800-222-1222 for questions or management guidance.

Counterfeit alprazolam

Did you know?

Nitazenes are frequently detected with other substances, especially in fatal overdoses.

Benzodiazepines, most often flualprazolam and etizolam, were detected in 82% of isotonitazene-related fatalities. Fentanyl and fentanyl analogs were found in 58% of isotonitazene fatalities, and cocaine was detected in 32% of cases. Methadone and benzodiazepines have also been detected in fatal overdoses of other drugs of the nitazene class, such as etonitazene. Additionally, nitazenes may be found in combination with each other, such as one fatal case of an overdose in Ohio, where both metonitazene and butonitazene were detected. The most common autopsy findings of fatal nitazene overdoses, reported in 8 cases, were lung congestion/edema, cardiomegaly/high cardiac weight, cerebral edema, presence of gastric contents in airways, and organ congestion. (Montanari *et al.*, 2022)

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