March 18, 2024

N-desethyl etonitazene and protonitazepyne: "New" nitazene opioids circulating in Toronto's unregulated opioid supply

For the first time, **Toronto's Drug Checking Service** has identified N-desethyl etonitazene and protonitazepyne in Toronto's unregulated opioid supply.

N-desethyl etonitazene and protonitazepyne are high-potency synthetic nitazene opioids. N-desethyl etonitazene is considered to be **up to 10 times stronger than fentanyl**. Protonitazepyne, also known as N-pyrrolidino protonitazene, is considered to be **more than 20 times stronger than fentanyl**.

N-desethyl etonitazene was first identified by our analysis site member at the **Centre for Addiction and Mental Health** (Clinical Laboratory and Diagnostic Services) on February 23, 2024. The sample was collected in Toronto's west end by our collection site member at **the Queen West Site of Parkdale Queen West Community Health Centre**. The sample was a yellow/beige powder that was expected to be (i.e., got or bought as) fentanyl. The sample did not contain fentanyl – it instead contained N-desethyl etonitazene and caffeine. Toronto's Drug Checking Service does not currently quantify N-desethyl etonitazene and therefore cannot speak to how much of it was present in the sample. The sample was not reported as being associated with an overdose or other unpleasant or abnormal effects.

Protonitazepyne was first identified by our analysis site member at the Centre for Addiction and Mental Health (Clinical Laboratory and Diagnostic Services) on March 6, 2024, and again the following day on March 7. The samples were collected in Toronto's west end by our collection site member at **the Parkdale Site of Parkdale Queen West Community Health Centre**. The samples were blue powders that were expected to be oxycodone (OxyContin). The samples did not contain oxycodone – they instead contained protonitazepyne and etonitazepyne (also known as N-pyrrolidino etonitazene and considered to be **more than 20 times stronger than fentanyl**). Toronto's Drug Checking Service does not currently quantify protonitazepyne or etonitazepyne and therefore cannot speak to how much of them were present in the samples. The samples were not reported as being associated with an overdose or other unpleasant or abnormal effects.

What are nitazene opioids?

Nitazene opioids were synthesized in the 1950s to relieve pain but were never clinically approved for market. Most nitazene opioids are considered to be stronger than fentanyl – and therefore classified as "high-

potency opioids" by Toronto's Drug Checking Service. Around 2019, nitazene opioids began presenting in the unregulated drug supply in Europe, the United States, and then Canada. In Canada, nitazene opioids have been especially prevalent in the eastern provinces – primarily Ontario and Quebec.

Toronto's Drug Checking Service first identified a nitazene opioid in Toronto's unregulated fentanyl supply in February 2021. Between February 12, 2021, and March 8, 2024, Toronto's Drug Checking Service:

- Has identified 10 different nitazene opioids in samples checked, including 4'-hydroxynitazene, 5-aminoisotonitazene, etodesnitazene, etonitazene, etonitazepyne, isotonitazene/protonitazene, metonitazene, N-desethyl etonitazene, N-desethyl isotonitazene, and protonitazepyne. You can learn more about these drugs, including their suspected strength as compared to fentanyl in our **Drug Dictionary**.
- Has reported nitazene opioids 555 times in 474 samples. The vast majority of these samples were expected to be fentanyl (418 of 474).
- Has observed **significant variation in the number of expected fentanyl samples that contain nitazene opioids**. Between January 1 and March 8, 2024, nitazene opioids were found in 3% of the expected fentanyl samples checked, as compared to 22% between January and March 2022.
- Has found nitazene opioids in 25 other expected opioid samples, including those expected to be oxycodone (OxyContin) (9 of 474), Percocet (5 of 474), hydromorphone (Dilaudid) (4 of 474), heroin (3 of 474), and hydrocodone (2 of 474). Two samples containing nitazene opioids were expected to be a nitazene opioid.
- Has not confirmed nitazene opioid contamination in samples that were expected to be other drug types, such as stimulants, psychedelics, dissociatives, or depressants.

What are the potential effects of using N-desethyl etonitazene and protonitazepyne?

- **Since N-desethyl etonitazene and protonitazepyne are so strong, the risk of overdose in increased and greater than normal doses of naloxone may be required to rouse individuals experiencing an overdose**.
- The risk of overdose may be further increased for people who use oxycodone (OxyContin), Percocet, hydromorphone (Dilaudid), or hydrocodone, as compared to people who use fentanyl, because their opioid tolerance may be lower.
- In expected fentanyl samples, high-potency opioids are often found in combination, likely increasing the strength of the opioids being used and, therefore, increasing the risk of overdose. For example, between January 1 and March 8, 2024, 42% of the expected fentanyl samples checked by Toronto's Drug Checking Service contained more than one high-potency opioid.
- In expected fentanyl samples, high-potency opioids are often found in combination with other central nervous system and/or respiratory depressants, such as benzodiazepine-related drugs and veterinary tranquilizers. For example, between January 1 and March 8, 2024, 58% of the expected fentanyl samples

checked by Toronto's Drug Checking Service contained at least one benzodiazepine-related drug and/or veterinary tranquilizer. Using high-potency opioids in combination other central nervous system and/or respiratory depressants increases the risk of dangerous suppression of vitals (e.g., slowing down of breathing, blood pressure, heart rate).

Advice to reduce potential harms associated with using N-desethyl etonitazene and protonitazepyne:

1. **Carry and be trained to use naloxone**. N-desethyl etonitazene and protonitazepyne are opioids, meaning naloxone should reverse their effects in an overdose situation. However, since N-desethyl etonitazene and protonitazepyne are so strong, greater than normal doses of naloxone may be required to rouse individuals experiencing an overdose. **Oxygen is often also provided in community health settings as a comprehensive overdose response**, specifically when benzodiazepine-related drugs and/or veterinary tranquilizers are present, and overdoses are therefore only partially reversed with naloxone.
2. **Get your drugs checked**, ideally before using, and providing services are available to you.
3. **Use at a supervised consumption site or overdose prevention site – or with someone else and take turns spotting each other**.
4. **If you must use alone, let someone know before you use.**
5. **Do a small test dose** first.
6. If your drugs did not contain what you were expecting, **consider talking to the person you got your drugs from**, or get your drugs from another source if possible.

View more **general harm reduction tips and help on our website**.

Which drug checking technologies can identify N-desethyl etonitazene and protonitazepyne at this time?

- Our analysis site member at the Centre for Addiction and Mental Health (Clinical Laboratory and Diagnostic Services) has identified N-desethyl etonitazene and protonitazepyne using liquid chromatography-Orbitrap high resolution mass spectrometry (LC-HR-MS).
- Our analysis site member at **St. Michael's Hospital** (Department of Laboratory Medicine) has identified N-desethyl etonitazene and protonitazepyne using gas chromatography-mass spectrometry (GC-MS).
- **Health Canada's Drug Analysis Service** (DAS) has identified protonitazepyne using GC-MS, nuclear magnetic resonance spectroscopy (NMR), and gas chromatography-infrared spectroscopy (GC-IR) in samples submitted by Canadian law enforcement agencies and public health partners. They have not yet identified N-desethyl etonitazene.

- N-desethyl etonitazene and protonitazepyne are not currently included in the library for the paper spray-mass spectrometer (PS-MS) used by the University of Victoria's **Substance** project, however, they are in the process of updating their library.
- Some Fourier transform infrared spectrometer (FTIR) libraries, such as **Kykeon Analytics'**, include protonitazepyne. However, it is likely that protonitazepyne would account for less than 5% of the sample, meaning it would fall below the FTIR's limit of detection and therefore be missed by instrument. To minimize this limitation, FTIR is often coupled with test strips, which are more likely to identify substances in trace amounts. Based on publicly available information, it is unlikely nitazene test strips can identify N-desethyl etonitazene and protonitazepyne.
- It is unlikely that emerging onsite drug checking technologies can identify N-desethyl etonitazene and protonitazepyne at this time as their libraries are being developed and their limits of detection are being determined.

Toronto's Drug Checking Service is a free and anonymous public health service that aims to reduce the harms associated with substance use and, specifically, to prevent overdose by offering people who use drugs timely and detailed information on the contents of their drugs. Beyond educating individual service users, results for all samples are collated and analyzed to perform unregulated drug market monitoring, then translated and **publicly disseminated every other week** to communicate unregulated drug market trends to those who cannot directly access the service, as well as to inform care for people who use drugs, advocacy, policy, and research. **Sign up** to receive reports, alerts, and other information on Toronto's unregulated drug supply.

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TORONTO Public Health

MOSS PARK OPS

PARKDALE QUEEN WEST Community Health Centre

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camh Centre for Addiction and Mental Health