

# The National Centre for Clinical Research on Emerging Drugs

## Emerging drug briefing

### Increasing reports of nitazene toxicity in Australia

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## Summary

- The purpose of this brief report is to inform public health professionals and policy makers of the emerging impact of nitazenes in the Australian illicit drug supply.
- Nitazenes are a group of highly potent synthetic opioids, up to 1000 times more potent than morphine by some measures.
- Nitazenes have been presented / taken as non-opioid drugs, for example MDMA, ketamine and benzodiazepines, presenting a risk of opioid overdose in non-opioid using populations.
- Naloxone is effective in the reversal of nitazene toxicity, and multiple doses may be necessary.
- Fentanyl strips will not detect nitazenes. Drug checking services can be used to detect nitazenes.
- Other harm reduction measures for opioid use (not using alone, staggering use in groups, avoid mixing different drugs) and effective access to treatment for opioid use disorder also reduce the risk of harms from nitazene poisoning.

## Nitazenes



Nitazenes (also called 2-benzyl-benzimidazoles) are a class of synthetic opioids which are highly potent opioid receptor agonists. Nitazenes range in their potency up to 1000 times (etonitazene) that of morphine (1,2), with new forms continuing to be identified (3). They were first developed in the 1950s as pharmaceutical products but were not feasible for clinical use due to their high potency. Nitazene toxicity presents similarly to other opioids with respiratory depression and decreased level of consciousness (4). In Australia, they were classified as a Schedule 9 Prohibited Substance under the current Poisons Standard by the Therapeutic Goods Administration in September 2023 (5).



**Table 1: Relative potency of selected nitazenes (6)**

Nitazene	Potency relative to morphine*
Butonitazene	5
Etodesnitazene	70
Metonitazene	100
Protonitazene	200
Isotonitazene	500
Etonitazene	1000

\*Antinociceptive potency relative to subcutaneous morphine in mice models (morphine = 1)

## **International Background**

Though there had been sporadic signals of etonitazene prior, nitazenes emerged as a current drug class of concern in 2019 in Europe (7) and North America (8) when isotonitazene was first detected. They continue to be associated with deaths and other harms in Europe (9,10), and the United States (11). New Zealand first detected nitazenes in March 2022, when etonitazepyne being sold as oxycodone were identified (12). Further alerts have been issued in New Zealand for metonitazene in October 2022 (13) and September 2023 (14), and protonitazepyne or isotonitazepyne in November 2023 (15). Significant reduction in opium production in Afghanistan may result in an increase of synthetic opioids in international markets (16), including Australia.

## **Nitazenes in Australia**

There have been several detections in Australia since the first reports in 2021. Case series of nitazenes presentation in that year have been published by the NSW Poisons Information (17) and Victorian emergency departments (18). Sentinel monitoring of emergency department presentations through Emerging Drug Network of Australia (EDNA) (19) has detected 22 nitazene cases (protonitazene, metonitazene, isotonitazene and etonitazepyne) in Queensland, South Australia, Victoria and Western Australia. The Drug Trends program at UNSW is currently preparing a report on nitazene detections through its Drugs and New Technologies monitoring program (20). Wastewater analysis has not yet detected nitazenes, though monitoring for new psychoactive substances is limited (21). Limited coronial data are currently publicly available, with three overdose deaths reported in Victoria in 2022 involving nitazenes (etonitazepyne, protonitazene and metonitazene) (22).

## **Drug Alerts**

Nitazene related harms, including death, have led to public drug alerts being issued in the Australian Capital Territory (23), New South Wales (24–27), Queensland (28), South Australia (29,30) and Victoria (31–33). There have also been detections in Western Australia through EDNA (19), and nitazenes have also been identified in police seizures in the Northern Territory (34). Nitazenes have been found represented as other opioids such as heroin (24) and oxycodone (23) and in non-opioid substances being sold as ketamine (31), MDMA (27), cocaine(32), alprazolam (28) and 3C-P (33).

**Table 2: Australian Public Drug Alerts for Nitazenes\***

	2022	2023	2024
<b>Australian Capital Territory</b>	Metonitazene (23)		
<b>New South Wales</b>	Etodesnitazene (25) Nitazene (25)	Isotonitazene (26)	Protonitazepyne(27)
<b>Queensland</b>		Protonitazene (28)	
<b>South Australia</b>		Protonitazene (29) Nitazenes (30)	
<b>Victoria</b>	Protonitazene (31)	Metonitazene (32)	Protonitazene (33)

\*Not all Australian jurisdictions issue public drug alerts

## Patterns of use

Nitazenes have been used intentionally or inadvertently through a range of routes of administration (oral, insufflation, inhalation, rectal, injection). The presence of nitazenes in non-opioid substances is of particular concern as people not intending to use an opioid may not use appropriate harm reduction measures such as carrying naloxone. They may also not be aware of harm reduction resources such as naloxone or how to deliver it.

## Responding to nitazenes

### Naloxone

As with other opioids, naloxone is effective at reversing nitazene toxicity in cases of overdose, although higher and/or repeated doses of naloxone may be required given the relatively high potency of nitazenes (35).

Promoting access and use of naloxone to reverse opioid toxicity in all situations where people may use illicit drugs, including the use of stimulants, is an important component of a comprehensive response. Naloxone may be required in situations where non-opioid drugs have been intended to be used.

### Drug checking & testing

Fentanyl test strips will not detect nitazene.

Where available, drug checking services can be used to enable people to reduce the risk of harm.

## Harm Reduction & Treatment Services

Harm reduction services provide an effective source of information and other services (such as take home naloxone) that prevent harms. Harm reduction messaging for opioids (avoid using alone, staggering use when using as a group, avoiding mixing drugs) is also appropriate for nitazenes.

Ensuring effective access to personalised treatment for opioid use disorder reduces the risk of non-medical opioid use.

## Communicating to the public

Broad dissemination of information about nitazenes to community supports the health, safety, and well-being of people who use drugs. Incorporation of lived experience expertise into communication design enhances the acceptability and uptake of messaging.

Effective media reporting reduces the likelihood of stigma and can enhance help-seeking. See Mindframe (36) for best practice language guidelines.

## Further resources

- [“What are nitazenes”](#) Australian Injecting & Illicit Drug Users League
- [“Nitazenes fact sheet”](#) Australian Drug Foundation
- Join [The Know Community](#) emerging drugs knowledge exchange platform to remain updated
- NCCRED webinars [Responding to emerging drugs of concern: nitazenes](#) (26 October 2023) and [Preparedness for Nitazenes](#) (27 March 2024)

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