

Emerging Drug Trends: Nitazenes, Tianeptine, and Synthetic Benzodiazepines

Substance use patterns are always changing. Drug use waxes and wanes over time, partly due to availability, price, attitudes, access, and the non-medical determinants of health. This brief focuses on nitazenes, tianeptine, and synthetic benzodiazepines. They are not the only emerging substances in the United States, and they may never reach national or regional prominence, but they have shown clear and dramatic increases over the past several years. Identifying emerging trends and addressing use before it becomes widespread can help reduce the scope and severity of drug epidemics.¹

HOW IS SUBSTANCE USE PREVALENCE ASSESSED?

Policymakers assess substance use prevalence using a combination of surveillance tools that include consumer surveys, overdose records, clinical and forensic drug-testing results, law enforcement statistics, and wastewater surveillance. Individually, each tool has strengths and limitations. But when combined, they can paint a clear picture of the state of substance use.

The United States has a robust research infrastructure with diverse data sources. This includes dozens of national surveys, such as the National Survey on Drug Use and Health, Monitoring the Future, and the Youth Risk Behavior Surveillance System. Fatal overdose records are available in the National

Vital Statistics System, and emergency department records of non-fatal overdoses are tracked by the Drug Abuse Warning Network. Drug-testing reports from national laboratories and drug availability assessments can also be accessed from the U.S. Drug Enforcement Administration (DEA) and U.S. Customs and Border Protection. Many states and cities also have infrastructure that enables researchers to conduct wastewater testing.

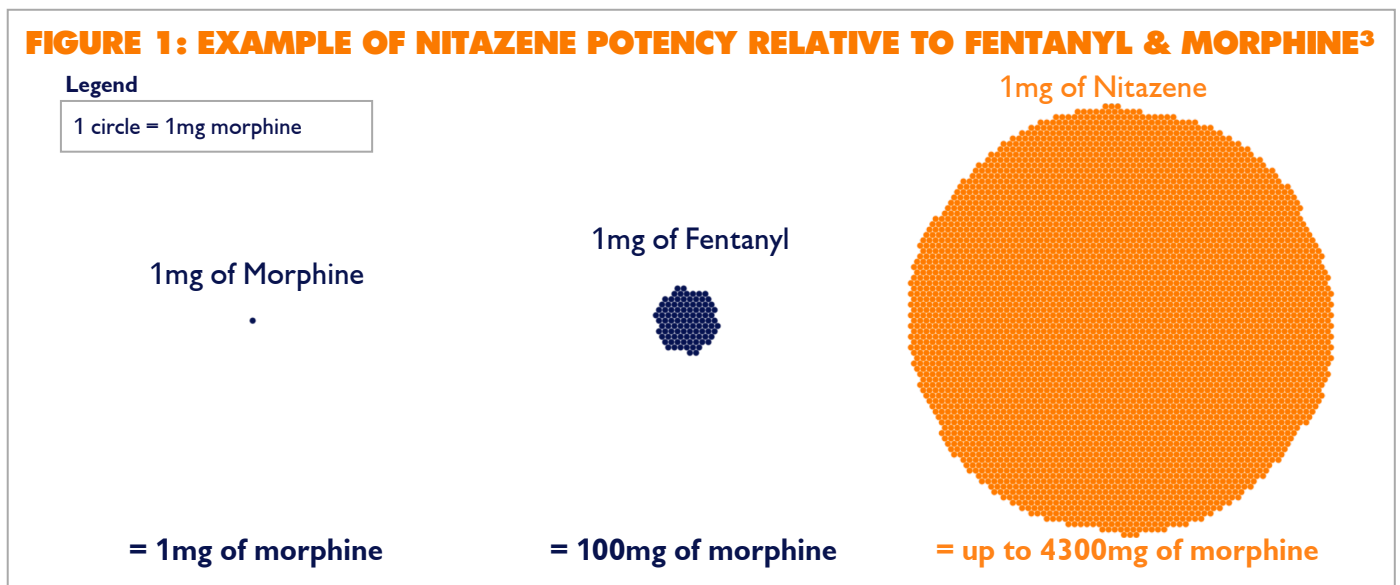
Emerging substances present a special challenge because they are rarely included in consumer surveys, clinical drug tests, or overdose records. Targeted wastewater surveillance, law enforcement data (i.e., seizures and arrests), and forensic drug-testing data can be more nimble. These more limited

tools often offer the first glimpse at emerging trends but can be less reliable than the full surveillance infrastructure.

NITAZENES

Nitazenes are the latest synthetic opioid to emerge as part of the ongoing opioid epidemic. They represent a dramatic increase in potency, even when compared with fentanyl. There are at least 13 different types of nitazenes, the most powerful of which are up to 43 times stronger than fentanyl (see Figure 1). The most widely available nitazene, isotonitazene or “ISO”, is approximately five to nine times stronger than fentanyl.² Fentanyl is roughly 100 times stronger than morphine — meaning that nitazenes can be up to 4,300 times stronger than morphine.

FIGURE 1: EXAMPLE OF NITAZENE POTENCY RELATIVE TO FENTANYL & MORPHINE³



Nitazenes were first identified in the U.S. illicit drug market in 2019. They are most commonly co-mingled within other substances, particularly other opioids and benzodiazepines, much as fentanyl is most often found within other opioids and stimulants. Nitazenes identified by the DEA are classified as Schedule I controlled substances.

Comprehensive nitazene prevalence data are unavailable. The standard consumer surveys do not ask about nitazenes, and laboratories and drug screenings do not commonly test for them. Comprehensive overdose data are also not available, but limited data from several states point to nitazene use as an emerging trend. Tennessee reported a large increase in nitazene-involved fatal overdoses, from 0 in 2019 to 42 in 2021.⁴ Limited wastewater testing also confirms use in Washington and Illinois.⁵ Additionally, law enforcement seizures point to growing nitazene prevalence in the illicit drug supply, with nitazenes found in at least 4,300 seizures since 2019.⁶

TIANEPTINE

First developed in the 1980s, tianeptine is used medically as an antidepressant and dietary supplement in some countries. Tianeptine is not approved by the U.S. Food and Drug Administration and is not currently federally controlled. At least 12 states have banned tianeptine, and Congress is considering legislation to classify it as a Schedule III drug. Although not an opioid, tianeptine acts as an agonist at the brain’s mu opioid receptors.⁷ When taken in large enough doses, it mimics the effects of opioids and poses a risk of addiction and overdose.⁸

FIGURE 2: INCREASE IN TIANEPTINE POISON CENTER CALLS 2000-2023



Tianeptine is colloquially known as “gas station heroin” because of its widespread availability at gas stations and convenience stores. Formal prevalence data are scarce, but calls to national poison centers have increased dramatically, from 11 in the 13-year period from 2000 to 2012 to 607 calls in the three years from 2020 to 2022.⁹ Growing numbers of published case reports also point to rising tianeptine use, as does tianeptine’s rising prominence on social media – a newer surveillance tool for emerging trends.¹⁰

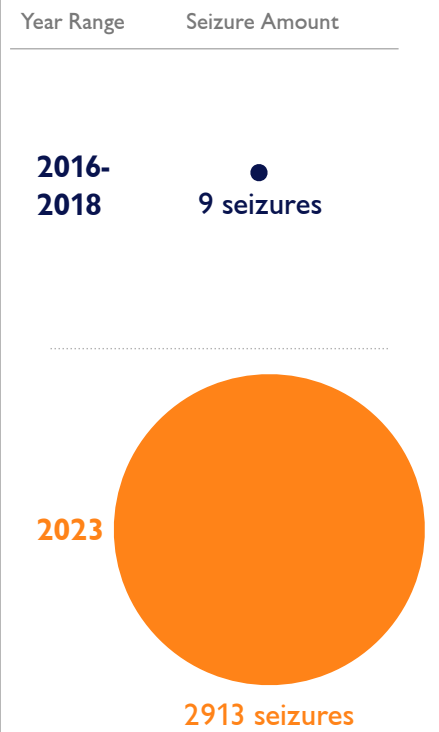
BROMAZOLAM AND OTHER SYNTHETIC BENZODIAZEPINES

Bromazolam, a benzodiazepine synthesized in 1976, was never marketed or approved for therapeutic use.¹¹ It first appeared in the U.S. illicit drug market in 2019, most frequently mixed with fentanyl. Due to its sedative effects, bromazolam poses significant health risks, especially when consumed with opioids. Bromazolam remains uncontrolled at the federal level, even though the DEA temporarily classified five other synthetic benzodiazepines as Schedule I in July 2023 and took steps to reduce their importation into the United States.¹² Since the change, bromazolam has become the most prevalent example of the growing

trend in synthetic benzodiazepine misuse across the United States.¹³

Comprehensive data on synthetic benzodiazepines remain scarce, but available evidence indicates a rapid emergence. Illinois reported a massive increase in bromazolam-involved deaths, up from 10 in 2021 to 51 in 2022.¹⁴ Law enforcement seizures for bromazolam have also dramatically increased since 2018, rising from roughly three seizures per year in 2016-2018 to 2,913 seizures in 2023.¹⁵

FIGURE 3: RISE IN BROMAZOLAM SEIZURES 2016-2023



Emerging Drug Trends: Nitazenes, Tianeptine, and Synthetic Benzodiazepines

Lab testing also points to an emerging trend. One national forensic lab found that the share of seized fentanyl containing bromazolam increased from 1% in Q1 2021 to 13% in Q2 2022.¹⁶ The same lab found increased use, with positive bromazolam tests growing from fewer than five in Q4 2020 to 60 in Q1 2022.

CONCLUSION

Nitazenes, tianeptine, and bromazolam are just three examples of newly emerging substances in the U.S, including xylazine, medetomidine, fluorofentanyl, and synthetic cannabinoids. Policymakers and practitioners should continue to monitor these and other emerging trends to help address potentially new patterns of substance use.

NOTES:

1. Winkler, D. et al (2004). Estimating the relative efficiency of various forms of prevention at different stages of a drug epidemic. *Socio-Economic Planning Sciences* 38(1). <https://www.sciencedirect.com/science/article/abs/pii/S0038012103000272>
2. Holland, A., et al. (2024). Nitazenes: Heralding a second wave for the UK drug-related death crisis? *The Lancet Public Health*, 9(2). [https://doi.org/10.1016/s2468-2667\(24\)00001-x](https://doi.org/10.1016/s2468-2667(24)00001-x)
3. Walton, S. (2023). *The newest wave of nitazene analogues* [Webinar]. CFSRE. https://www.cfsre.org/images/Presentations/WaltonSE_NPS_Quarterly_Webinar_230705SW.pdf
4. Roberts, A., et al. (2022). Notes from the field: Nitazene-related deaths – Tennessee, 2019-2021. *MMWR*, 71(37), 1196-1197. <https://doi.org/10.15585/mmwr.mm7137a5>
5. Bade, R., et al. (2022). Wastewater-based monitoring of the nitazene analogues: First detection of protonitazene in wastewater from the United States. *Therapeutic Drug Monitoring*, 44(4). <https://doi.org/10.2139/ssrn.4625819>
6. US DEA. (2024). Benzimidazole-opioids. Other name: Nitazenes. https://www.deadiversion.usdoj.gov/drug_chem_info/benzimidazole-opioids.pdf
7. US DEA (2024). *Tianeptine* https://www.deadiversion.usdoj.gov/drug_chem_info/tianeptine.pdf
8. Zahran, T.E. et al (2018). Characteristics of Tianeptine Exposures Reported to the National Poison Data System – United States, 2000-2017. *MMWR* 67(30); 815-818. <https://www.cdc.gov/mmwr/volumes/67/wr/mm6730a2.htm>
9. US DEA (2024). *Tianeptine* https://www.deadiversion.usdoj.gov/drug_chem_info/tianeptine.pdf
10. Edinoff, A. et al. (2023). Tianeptine, an Antidepressant with opioid Agonist Effects: Pharmacology and Abuse Potential, a Narrative Review. <https://link.springer.com/article/10.1007/s40122-023-00539-5>
11. WHO (2023). Critical review report: Bromazolam. https://cdn.who.int/media/docs/default-source/46th-ecdd/bromazolam_46th-ecdd-critical-review_public-version.pdf
12. US DEA (2023). Five Synthetic Benzodiazepine Drugs Deemed Imminent Hazard to Public Safety. <https://www.dea.gov/stories/2023/2023-09/2023-09-25/five-synthetic-benzodiazepine-drugs-deemed-imminent-hazard-public>
13. Papsun, D. (2023). Bromazolam—the Most Frequently Identified NPS Benzodiazepine in 2023. CFSRE. https://www.cfsre.org/images/Presentations/NPS_Discovery_Bromazolam_Papsun_July_2023.pdf
14. Ehlers, P. et al (2024). Notes from the Field: Seizures, Hyperthermia, and Myocardial Injury in Three Young Adults Who Consumed Bromazolam Disguised as Alprazolam – Chicago, Illinois, February 2023. *MMWR* 72(5253); 1392-1393. <https://www.cdc.gov/mmwr/volumes/72/wr/mm725253a5.htm>
15. Ehlers, P. et al (2024). Notes from the Field: Seizures, Hyperthermia, and Myocardial Injury in Three Young Adults Who Consumed Bromazolam Disguised as Alprazolam – Chicago, Illinois, February 2023. *MMWR* 72(5253); 1392-1393. <https://www.cdc.gov/mmwr/volumes/72/wr/mm725253a5.htm>
16. CFSRE. (2022). Bromazolam Prevalence Surging Across the United States in Part by Increasing Detections Alongside Fentanyl. https://www.cfsre.org/images/content/reports/public_alerts/Public-Alert_Bromazolam_NPS-Discovery_061522.pdf



This Info Brief is a publication of Carnevale Associates, LLC. Carnevale Associates brings strategic consulting solutions to governments, organizations, and communities as they confront the policy and program challenges of substance use, behavioral health, and criminal justice. www.carnevaleassociates.com