Cychlorphine: An Emerging Threat in the Illicit Drug Supply

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Background

In recent years, the rapid evolution of the illicit drug market has led to the proliferation of novel synthetic opioids (NSOs), many of which pose substantial public health risks. Among these, cychlorphine has emerged as a concerning new substance in the illicit drug supply due to its high potency, expanding geographic spread, and presence in polysubstance drug mixtures.[1] As the illicit drug supply continues to change, access to timely and accurate information on related substances remains a critical component of harm reduction and can effectively save lives. In the first quarter of 2026, The Center for Forensic Science Research and Education (CFSRE) identified NSOs in 32% of all identified submissions related to novel psychoactive substances (stimulants, hallucinogens, benzodiazepines, and synthetic cannabinoids) (Ref: NPS opioids).[2]

Data from the CFSRE 2026 Q1 show the percentages of drugs within a particular class that were detected (opioids include cychlorphine, nitazene, brorphine, etc) (Figure 1). The numbers presented above do not include fentanyl itself (over 800 samples contained fentanyl in addition to the other NSOs).

What is Cychlorphine?

Cychlorphine, formally known as N-propionitrile chlorphine, is an NSO that was first identified in the United States by the CFSRE in August 2024 and confirmed in September 2024.[1] Cychlorphine is part of a new wave of synthetic opioids that are increasingly being detected in illicit drug markets, often through signals such as clusters of overdoses or poison center calls accompanied by specimen submission to CFSRE. These substances often develop much faster than standard drug detection systems are updated.[3] Cychlorphine is a brorphine analog belonging to a broader emerging class of NSOs called the "orphines." Orphines first emerged in recreational drug markets in 2020 with the proliferation of brorphine, a potent synthetic opioid that was reported to the United Nations Office on Drugs and Crime (UNODC) Early Warning Advisory in 2019.[4] As a class, orphines have undergone significant diversification with the introduction of six new analogs confirmed in recent years, including N-propionitrile chlorphine. Cychlorphine bears a structural resemblance to certain benzimidazolones, including brorphine, chlorphine, and florphine (Figure 2), but differs structurally from other nitazene opioids.[5] Specifically, nitazene opioids (2-benzylbenzimidazole) are chemically and structurally distinct from brorphine-like opioids (piperidine benzimidazolone), such as cychlorphine, although both are benzimidazolones.[6]

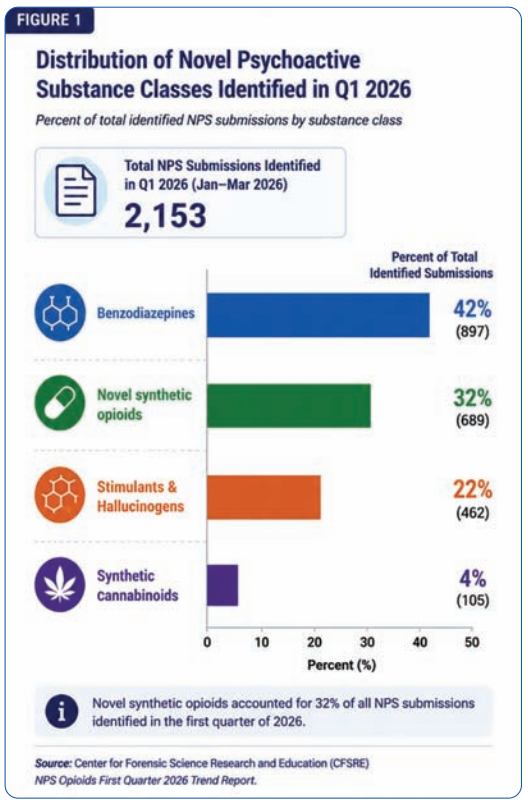
Comparison to Fentanyl

Cychlorphine is thought to have a potency similar to or higher than fentanyl, and it represents a significant threat to the illicit drug supply due to its very high potency. Additionally, it is being detected as the sole opioid in counterfeit opioid tablets labeled as hydromorphone or oxycodone, as of 2025 in Toronto.[7] Like other NSOs, cychlorphine is believed to bind to mu-opioid receptors in the brain, producing effects similar to fentanyl and other related substances.[8] Additionally, cychlorphine is frequently encountered in combination with other drugs, including NSOs and stimulants, similar to fentanyl.[1] When multiple substances are involved, overdose risk becomes more complex since naloxone is only effective with opioids.[3] While naloxone is the most important antidote, it will reverse respiratory and other effects from opioids, not the effects from nonopioid agents in polydrug overdoses/use, which have become extremely common if not the norm in the emergency departments (EDs) and prehospital settings. It is also important to consider the hypercapnia that develops with inadequate ventilation periods during overdose. Postmortem data also confirm multiple substances often detected along with an opioid when one is present (in particular, synthetic opioids). Although cychlorphine shares functional characteristics with fentanyl, it differs structurally, belonging to a different group of synthetic opioids. Notably, according to in vitro pharmacology data, cychlorphine has been reported to be approximately 10 times more potent than fentanyl, causing rapid respiratory depression.[1]

FIGURE 1

Distribution of Novel Psychoactive Substance Classes Identified in Q1 2026

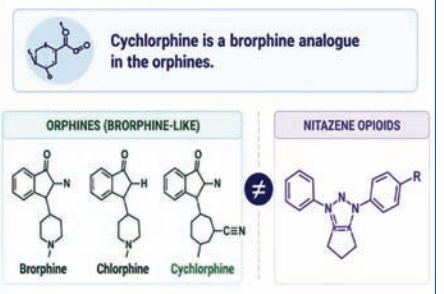
Percent of total identified NPS submissions by substance class



Source: Center for Forensic Science Research and Education (CFSRE)
NPS Opioids First Quarter 2026 Trend Report.

FIGURE 2

Structural Relationships of Cychlorphine Within the Orphines and Compared to Nitazene Opioids



At present, no commercially available drug-checking test strips are specifically designed to detect cychlorphine (fentanyl test strips do not reliably detect). While cross-reactivity with standard fentanyl test strips may occur, detection is not reliable or well characterized, limiting the ability of individuals and harm reduction programs to identify cychlorphine exposure in real time.[9] This challenge extends to many emerging NSOs, adulterants, and contaminants in the illicit drug supply, many of which are psychoactive and may contribute to additive or compounding overdose effects.

Geographic Distribution of Cychlorphine

Cychlorphine has been detected across an increasingly broad geographic range, indicating its diffusion through established drug trafficking networks rather than confinement to isolated regions. The CFSRE has reported the detection of cychlorphine in 100 toxicology specimens across multiple U.S. states and three Canadian provinces since 2024, suggesting cross-border distribution throughout North America.[1] Within the United States, the substance has been documented along the East Coast as well as in states including California, Texas, Kentucky, Ohio, Illinois, Tennessee, Pennsylvania, Nevada, New York, Louisiana, and Connecticut.[1] Beyond these U.S. regions, cychlorphine has been detected in major international cities such as London, Toronto, and Montreal (Figure 3), further emphasizing its increasing global presence in both Europe and Canada.[8] Cychlorphine has been detected in various labs, including the CFSRE, NMS Labs, DEA Labs, the NC Opioid Data Lab, the National Institute of Standards and Technology (NIST), and the Knox County Regional Forensic Center. While cychlorphine is generally understood to be introduced into the illicit drug supply as an additive rather than as a standalone substance, raising concerns about widespread inadvertent exposure, recent findings suggest this may not always be the case.[9] The CFSRE has identified several overdose deaths in which cychlorphine was the only opioid detected, indicating a potential shift or variation in how it is appearing in the supply.[10]

Use of Naloxone in Cychlorphine-Related Overdoses

Due to cychlorphine's high potency and unreliable detection with current drug test strips, there is an elevated risk of unintentional overdose. As with other opioids, naloxone remains an effective intervention for reversing opioid overdose. Because naloxone consistently acts on the same opioid receptors, there is no publicly available evidence indicating that naloxone is any less effective at reversing a cychlorphine-related overdose than overdoses involving other opioids.[10] This corrects a widespread misconception that arose from a mix-up between cychlorphine and chlorphine, a different substance, in a study regarding pretreatment blocking that suggested naloxone's ineffectiveness in the treatment of opioid overdoses.[10] Importantly, naloxone works on opioid receptors rather than the opioid compounds themselves, meaning that increased potency does not inherently reduce naloxone's effectiveness. Guidance from the CFSRE emphasizes the importance of supportive treatment of cychlorphine overdose by treating the airway and breathing first, followed by judicious administration of naloxone, being careful not to precipitate acute withdrawal. In the prehospital setting, where airway management may be delayed and naloxone is often administered by laypersons or first responders, an initial higher dose of naloxone may be appropriate to rapidly respiratory depression and reduce the risk of underdosing. In a monitored setting (oxygen, end-tidal capnography, etc), careful titration can be performed to improve respirations without precipitating withdrawal (eg, 0.04 mg/mL naloxone IV every ~3 minutes until noted improvement and stabilization of breathing).[10]

Harm Reduction Strategies for Cychlorphine Exposure

Given the increasing presence of cychlorphine in the illicit drug supply, harm reduction strategies are critical to minimizing the risk of overdose and death. Because no commercially available test strips currently detect cychlorphine, individuals may be unknowingly exposed to the substance when it is mixed with other drugs, making precautionary measures especially important.[9] Individuals are advised to avoid using drugs alone or behind closed doors, as this could hinder timely detection and/or intervention in the event of an overdose. Services such as SafeSpot (1-800-972-0590), a hotline that remains on the phone during substance use and contacts emergency services if the caller becomes unresponsive,

FIGURE 3

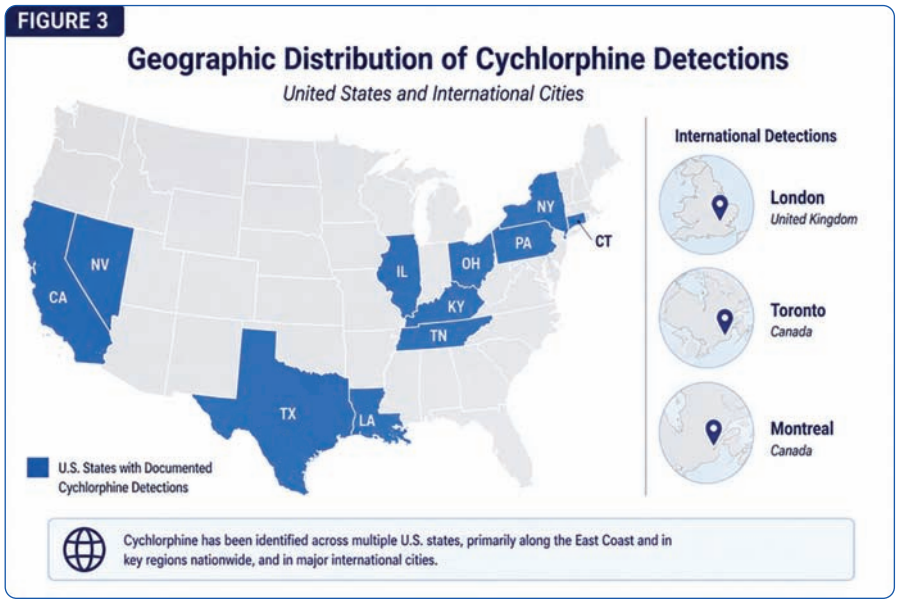
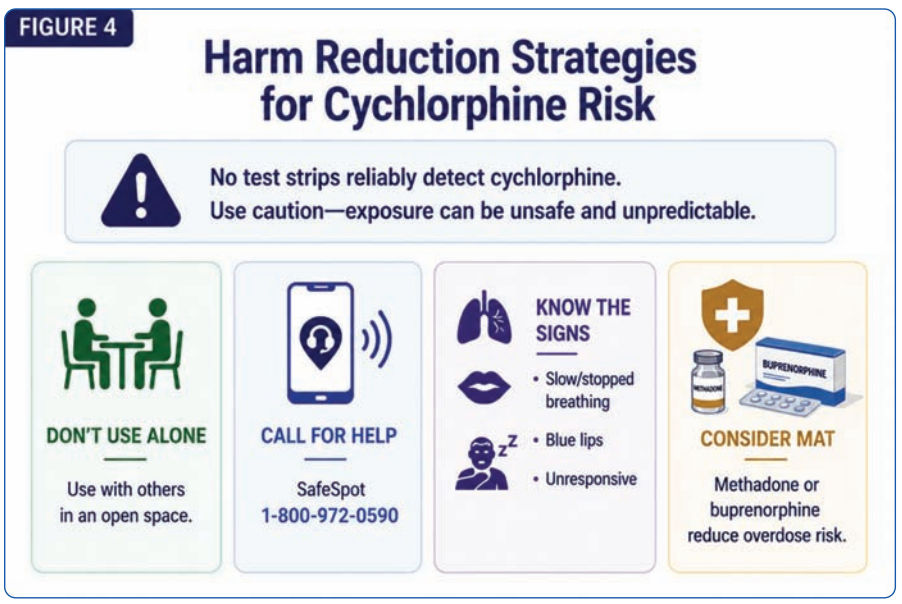


FIGURE 4



provide an additional layer of protection.[11] It is also vital to understand the signs of an overdose, which can include slow/stopped breathing, blue lips, and unresponsiveness. From a harm reduction perspective, participation in medication for addiction treatment involving methadone or buprenorphine remains one of the most protective factors against fatal overdose (Figure 4).[12]

Cychlorphine represents an evolving threat within the illicit opioid supply. Its high potency, expanding geographic distribution, limited test strip reliability, and presence within polysubstance mixtures create a substantial overdose risk. Continued toxicologic surveillance, clinician awareness, harm reduction expansion, and access to evidence-based addiction treatments are needed. **EMN**

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POCUS: The Probe Helps. The Proof is Trickier

By Christine Butts, MD; Paul Butts, MD

Most first year emergency medicine residents have at least basic facility with point of care ultrasound (POCUS). Many have skills far beyond what would have been considered adequate for a graduating EM resident 20 years ago. We ultrasound everything from optic nerves to metatarsal joints, but does it actually improve patient care?

Let's start with the good news: what we know POCUS does well.

Ultrasound often cuts out the middleman. Instead of waiting for a lab test or a read by radiology, we get answers in seconds at the bedside. In patients with concern for pregnancy complications, POCUS shortened the time to diagnosis of intrauterine pregnancy by 72 minutes when compared with radiology-performed ultrasound.[1] A diaphoretic patient with chest pain can be a lot of things but a quick ultrasound that identifies a dilated aortic root can help focus care quickly, limiting time chasing other diagnoses.

Ultrasound improves procedural success. POCUS efficacy for placement of

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central lines is well known, but it also aids peripheral intravenous (IV) placement, improving overall success, first attempt success, and decreased overall time.[2] A 2025 meta-analysis of randomized controlled trials in pediatric emergency departments (EDs) demonstrated that POCUS improved both first attempt and overall procedural success, including IV access and lumbar puncture.[3]

Unfortunately, there has been less demonstration of morbidity or mortality benefit. Notably, the SHOC-ED trial (covered in Speed of Sound in January 2019) found that adding POCUS to the evaluation of undifferentiated shock did not add much in the terms of survival, length of stay, or several other metrics.[4]

Designing studies that meet stringent criteria to establish a mortality benefit can be difficult. A critical review from 2025 found most POCUS studies focus on accuracy and less on outcome, preventing a full assessment of its impact.[5] It also highlighted other issues impeding the adoption of POCUS: image acquisition, adequate training, and oversight. If you perform a FAST in the trauma bay and don't save the images, was it ever performed at all?

Where does this leave us? POCUS is here to stay but how do we justify its existence? Should we even try? You don't see trials justifying the mortality benefit of a stethoscope.

I go back to how I have always considered POCUS. As emergency physicians, so much of what we do is based on pattern recognition plus some data, but we don't typically have the whole picture. A tool that is available, increasingly accepted, and doesn't depend on another department for results can be invaluable in putting a patient that would otherwise be undifferentiated onto a beneficial care pathway early in the treatment course. Additionally, although mortality benefit might be tough to demonstrate, improving throughput, decreasing time to disposition, and improving first pass procedure success mean a lot to your everyday community ED physician. **EMN**

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