

Potent Synthetic Opioid - Isotonitazene - Recently Identified in the Midwestern United States

Purpose: The objective of this public announcement is to notify public health and public safety, law enforcement, clinicians, medical examiners and coroners, laboratory personnel, and all other related communities about new information surrounding the emergent synthetic opioid isotonitazene.

Background: Synthetic opioids are chemically manufactured drugs, often associated with unknown biological effects and health risks, a dangerous combination for any recreational drug user. Synthetic opioids are often prepared in powder or tablet form and can be mixed with street level traditional opioids. In the United States, a staggering number of deaths have been reported in recent years linked to synthetic opioid use. The primary adverse effect most commonly reported in association with synthetic opioid use is respiratory depression, often leading to death.

Summary: Isotonitazene is a potent synthetic opioid bearing structural resemblance to etonitazene, a synthetic opioid that is nationally and internationally controlled. Isotonitazene is dissimilar in structure to popular synthetic opioids typically encountered in forensic casework (e.g. fentanyl analogues, U-series analogues). Isotonitazene and similar analogues (e.g. etonitazene, metonitazene, and clonitazene) were first synthesized and reported in the literature in the 1950s. Pharmacological data suggest that this group of synthetic opioids have potency similar to or greater than fentanyl based on their structural modifications. Etonitazene is reported to be the most potent of the group followed by isotonitazene and metonitazene. The toxicity of isotonitazene has not been extensively studied but recent association with drug user death leads professionals to believe this new synthetic opioid retains the potential to cause widespread harm and is of public health concern. Isotonitazene has been identified in eight blood specimens associated with postmortem death investigations in the United States since August 2019. Isotonitazene was first reported in August 2019 based on the results from seized drug and toxicology casework in Europe (Belgium) and Canada (Alberta); the Canadian toxicology case was collected in March 2019.

Demographics

Age:

- Avg. 42, Med. 42.5
- Range: 20's to 60's

Sex:

- Male (n=6), Female (n=2)

Case Type:

- Postmortem (n=8)

Specimen Type:

- Blood (n=8)

Date of Collection:

- Aug. to Oct. 2019

Other Notable Findings:

- Etizolam (n=6)
- Fentanyl (n=3)
- U-47700 (n=1)
- Piperidylthiambutene (n=1)

Recommendations for Public Health

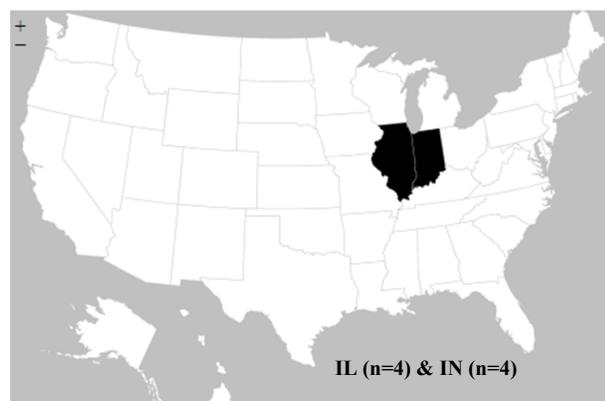
- Implement surveillance for rapid identification of drug overdose outbreaks.
- Engage local poison centers and clinicians to assist with treatment of affected patients.
- Track and monitor geographical drug distribution and trends.
- Track demographics and known risk factors for decedents and overdose patients.
- Raise awareness about the risks and dangers associated with opioid use.
- Make naloxone available to recreational drug users.

Recommendations for Clinicians

- Become familiar with the signs and symptoms associated with synthetic opioid use (e.g. sedation, respiratory depression).
- Naloxone should be administered to reverse critical respiratory depression. Be aware that clinical conditions may change rapidly and unpredictably after naloxone administration due to precipitation of withdrawal.
- Be mindful that illicit drugs have limited quality control, containing undeclared substances that impact the expected clinical effects or findings.
- Counsel about the dangers of synthetic opioid products and other drugs.

Recommendations for MEs & Coroners

- Test for new synthetic opioids and their biomarkers in suspected opioid overdose cases.
- Be aware that ELISA screening for synthetic opioids may not be specific or specialized for the newest generation of compounds; consider mass spectrometry-based screening.
- Be aware that concentrations of synthetic opioids in biological specimens can vary and GC-MS sensitivity may not be adequate.



Recommendations for Laboratories

- Utilize analytical data available publicly for the identification of isotonitazene and other synthetic opioids if reference standards are not available.
- Utilize previously developed non-targeted testing protocols or develop sensitive and up-to-date testing procedures for synthetic opioids.
- Prioritize analytical testing of seized drug samples taken from drug overdose scenes during death investigations.
- Share data on synthetic opioid drug seizures with local health departments, medical examiners, and coroners.

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References and Related Articles:

- Hunger, A; Kebrle, J; Rossi, A; Hoffmann, K. (1957) [Synthesis of analgesically active benzimidazole derivatives with basic substitutions. *Experientia*, 13, 400-401.](#)
- Hoffmann, K; Hunger, A; Rossi, A. (3 May 1960). [Patent US2935514A - Benzimidazoles.](#)
- [Police warning of new deadly opioid found on Calgary streets](#)
- CDC: [Synthetic Opioid Overdose Data](#)

Rapid NPS Testing Now Available:

If your agency suspects synthetic opioid toxicity with no identifiable cause of death or your jurisdiction is noticing an increase in overdose patients requiring analytical testing, contact NPS Discovery at the Center for Forensic Science Research and Education; a non-profit organization in collaboration with DOJ and CDC, which has received funding to provide rapid testing of novel drug outbreaks in the United States.

Website: npsdiscovery.org Email: npsdiscovery@frfoundation.org