New High Potency Synthetic Opioid N-Pyrrolidino Etonitazene (Etonitazepyne) Linked to Overdoses Across United States

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

Background: Synthetic opioids are chemically manufactured drugs, often accompanied with unknown potency and adverse effects or health risks. New synthetic opioids may be mixed with more traditional opioids, creating additional risk and danger for recreational drug users. Synthetic opioids may be distributed in powder or tablet form. In the United States (U.S.), an alarming increase in the number of deaths linked to synthetic opioid use has been reported. The primary adverse effect associated with synthetic opioid use is respiratory depression, often leading to death.

Summary: N-Pyrrolidino etonitazene (etonitazepyne) is a new high potency synthetic opioid bearing structural resemblance to etonitazene, a synthetic opioid that is nationally and internationally controlled. N-Pyrrolidino etonitazene is dissimilar in structure to other synthetic opioids typically encountered in forensic casework (e.g., fentanyl). Unlike the 2-benzylbenzimidazole analogues that were first synthesized and reported in the literature in the 1950s (e.g., metonitazene, isotonitazone), N-pyrrolidino etonitazene does not appear in prior literature or patents. Recent in vitro pharmacological data suggest that this new opioid exhibits potency similar to etonitazene (~20x more potent than fentanyl). N-Pyrrolidino etonitazene was first reported by NPS Discovery in May 2021 following initial detection in a toxicology case. To date, eight blood specimens associated with postmortem death investigations in the U.S. have contained N-pyrrolidino etonitazene; additional confirmations are pending. The toxicity of N-pyrrolidino etonitazene has not been examined or reported but recent association with death among people who use drugs leads professionals to believe this synthetic opioid retains the potential to cause widespread harm and is of public health concern. Identifications of N-pyrrolidino etonitazene have also been reported recently from agencies in Europe.

References and Related Articles:
- Unpublished data from M. Vandeputte and C. Stove

Acknowledgements: This report was prepared by Alex J. Krutulski, PhD; Donna M. Papuan, MS, D-ABFT; Sara E. Walton, BS; and Barry K. Logan, PhD, D-ABFT. Funding was received from the National Institute of Justice (NIJ) of the U.S. Department of Justice (DOJ) (Award Number 2020-DQ-BX-0007). The opinions, findings, and conclusions or recommendations expressed in this publication are those of the authors and do not necessarily reflect those of the Department of Justice.

Geographical Distribution of N-Pyrrolidino Etonitazene

Case Type: 
- Postmortem (n=8)
- Age: Range: 20s to 50s
- Date of Collection: January to April 2021

Other Notable Findings:
- NPS Benzodiazepines (n=7)
- Fentanyl (n=4)
- Methamphetamine (n=4)
- *Only Drug of Interest (n=1)

<table>
<thead>
<tr>
<th>N-Pyrrolidino Etonitazene</th>
</tr>
</thead>
<tbody>
<tr>
<td>Case A</td>
</tr>
<tr>
<td>Case B</td>
</tr>
</tbody>
</table>

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 (CFSRE); a not-for-profit organization in collaboration with local and federal agencies, which can provide rapid testing after novel drug outbreaks in the United States.

Website: www.npsdiscovery.org Email: npsdiscovery@cfsre.org