









Emerging Threats Within the Opioid Crisis February 29, 2024



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- This webinar also has been approved by NJ OEMS for 1 EMT Elective CEU.
- Attendees seeking 1 EMT Elective CEU will be provided a link specific to EMTs to apply for credit at the end of the webinar and in the follow-up email tomorrow.
- Attendees seeking EMT credit must apply for credit within 30 days of today's webinar.

PA Planner Dean Barone discloses that he serves on the speakers bureau of Ethicon and Johnson & Johnson.



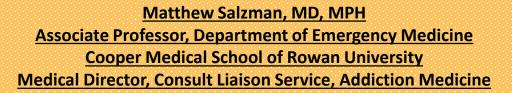
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- You must apply to receive continuing education credit. It will not be sent to you just for attending this webinar.
- WHERE CAN YOU FIND THE LINK TO APPLY FOR CREDIT?
 - The last slide of this webinar
 - The chat at the end of the program
 - The follow-up email you will receive tomorrow
- The poll at the end of today's webinar IS NOT the evaluation for continuing education credit. The evaluation will be at the link mentioned above.
- The link will be active for 30 days after today's event.



Featured Presenters





Matthew Salzman is an associate professor in emergency medicine at Cooper Medical School of Rowan University, as well as the medical director of the Addiction Medicine Consult Liaison Service at Cooper University Healthcare and the medical director of Research for the Division of Toxicology and Addiction Medicine. He also serves as a volunteer consultant in toxicology at the Children's Hospital of Philadelphia and the Philadelphia Poison Control Center. Dr. Salzman graduated from Jefferson Medical College and then completed residency training in emergency medicine at Drexel University College of Medicine. Upon completing residency, Salzman remained at Drexel as a fellow in medical toxicology. He recently graduated from the Master of Public Health program at the Bloomberg School of Public Health at Johns Hopkins University.



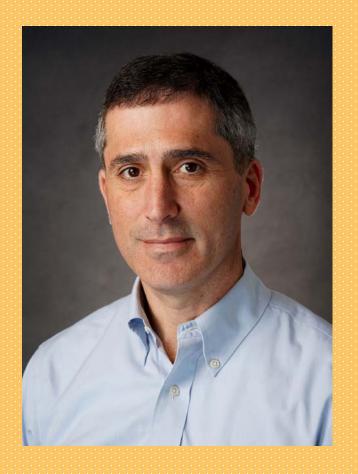
Bruce Ruck, Pharm.D., DABAT

Managing Director and Director of Drug Information
and Professional Education

New Jersey Poison Information and Education System

Bruce Ruck is the managing director of the New Jersey Poison Center, which is in the Department of Emergency Medicine at Rutgers New Jersey Medical School in Newark. Dr. Ruck graduated from St. John's University with a Bachelor of Science degree in pharmacy in 1986 and Doctor of Pharmacy degree in 1988. He then went on to complete a clinical Pharmacy Residency at Shands Hospital at the University of Florida in 1989. Dr. Ruck then joined Newark Beth Israel Medical Center in a split position between the Pharmacy and NJ Poison Center. He moved full-time to University of Medicine and Dentistry of New Jersey (UMDNJ), now Rutgers School of Biomedical and Health Sciences, in January 2002 with the poison center.





Matthew Salzman, MD, MPH

Associate Professor, Department of Emergency Medicine

Cooper Medical School of Rowan University

Medical Director, Consult Liaison Service, Addiction Medicine



XYLAZINE - THE TROUBLE WITH TRANQ

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DISCLOSURES AND OTHER INFO

- No financial conflicts of interest
- Classically trained musician
- Grant support
 - Camden Opioid Research Initiative
 - PCORI Kit Delgado, MD
 - NIDA CTN Gail D'Onofrio, MD





CASE FOR THE DAY

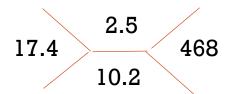






CASE FOR THE DAY - LABS

| 126 | 97 | 76 |
|-----|----|-----|
| 5.9 | 14 | 2.7 |



- Alk phos 322
- ESR>100
- CRP 15.94
- UDS +methadone, fentanyl
- Urine xylazine 9750 ng/mL
- Blood cx + Tissierella praeacuta





APRIL 12, 2023

Biden-Harris Administration Designates Fentanyl Combined with Xylazine as an Emerging Threat to the United States

→ ONDCP → BRIEFING ROOM → PRESS RELEASES



We're talking about fentanyl and xylazine all wrong

Rather than stigmatizing people living with addiction, the most important thing we can do is encourage and support people in their journey to recovery.

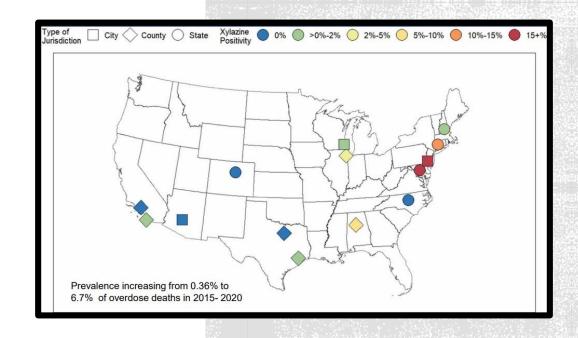


A Narcan kit in North Philadelphia on Wednesday, Dec. 14, 2022. Monica Herndon / Staff Photographer

by Jeanmarie Perrone, For The Inquirer Published Oct. 3, 2023, 5:00 a.m. ET ADVERTISEMENT



Xylazine Prevalence



Drug Alcohol Depend. 2022 April 01; 233: 109380. doi:10.1016/j.drugalcdep.2022.109380.

Xylazine spreads across the US: A growing component of the increasingly synthetic and polysubstance overdose crisis

Joseph Friedman^{a,b,*}, Fernando Montero^c, Phillippe Bourgois^a, Rafik Wahbi^d, Daniel Dye^e, David Goodman-Meza^f, Chelsea Shover^g



XYLAZINE GROWTH BY REGION

(U) Figure 1. DEA Forensic Laboratory Identifications of Xylazine by Region

| Region | 2020 | 2021 | Percent Increase |
|-----------|------|------|---------------------|
| Northeast | 346 | 556 | 61% |
| South | 198 | 580 | 193% |
| Midwest | 110 | 118 | 7% |
| West | 77 | 163 | 112% |

Source: DEA

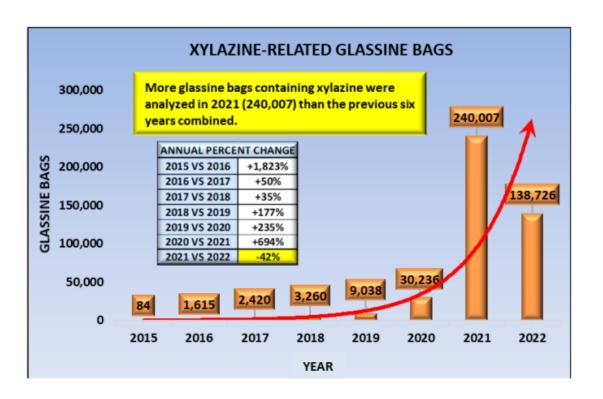
(U) Figure 2. Number of Xylazine-Positive Overdose Deaths by Region

| Region | 2020 | 2021 | Percent Increase | |
|-----------|------|-------|---------------------|--|
| Northeast | 631 | 1,281 | 103% | |
| South | 116 | 1,423 | 1,127% | |
| Midwest | 57 | 351 | 516% | |
| West | 4 | 34 | 750% | |

Source: DEA







| YEAR |) | KYLAZIN | E-RELATE | D | ALL SUSPECTED HEROIN | | |
|------|-------|------------------------|----------|-------------|----------------------|---------|--|
| TEAR | SUBMI | MISSIONS GLASSINE BAGS | | SUBMISSIONS | GLASSINE BAGS | | |
| 2015 | 9 | 0.1% | 84 | 0.01% | 13,170 | 590,051 | |
| 2016 | 55 | 0.4% | 1,615 | 0.3% | 12,750 | 576,698 | |
| 2017 | 47 | 0.4% | 2,420 | 0.5% | 11,399 | 504,293 | |
| 2018 | 88 | 1% | 3,260 | 1% | 12,387 | 583,399 | |
| 2019 | 368 | 3% | 9,038 | 1% | 13,010 | 680,807 | |
| 2020 | 855 | 11% | 30,236 | 6% | 7,814 | 500,715 | |
| 2021 | 3,055 | 30% | 240,007 | 29% | 10,344 | 821,180 | |
| 2022 | 2,595 | 36% | 138,726 | 29% | 7,272 | 474,681 | |

New Jersey Office of Drug Monitoring and Analysis Quarterly Report

October 1, 2022-December 31, 2022

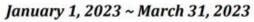


| XYL |
|-----|
| |
| 1% |
| 3% |
| 2% |
| 1% |
| 0% |
| 1% |
| 9% |
| 4% |
| 2% |
| 1% |
| 9% |
| 5% |
| 0% |
| 2% |
| 4% |
| 8% |
| 1% |
| 1% |
| 2% |
| 5% |
| 1% |
| |
| _ |

| XYLAZINE-RELATED GLASSINE BAGS | | | | | | | | | | | | |
|--------------------------------|------|-------|-------|-------|--------|-----------------|--------|--------|---------|--------|---------|------|
| COUNTY | 20 |)19 | 20 | 120 | 20 | 21 | 20 | 22 | 2023 (T | 03/31) | TOT | AL |
| ATLANTIC | 190 | 2% | 7,656 | 25% | 31,133 | 13% | 15,444 | 11% | 17,548 | 30% | 71,971 | 15% |
| BERGEN | 116 | 1% | 347 | 1% | 16,809 | 7% | 3,676 | 3% | 599 | 1% | 21,547 | 5% |
| BURLINGTON | 1046 | 12% | 2,003 | 7% | 5,647 | 2% | 6,088 | 4% | 543 | 1% | 15,327 | 3% |
| CAMDEN | 111 | 1% | 2,537 | 8% | 27,830 | 12% | 9,967 | 7% | 2,027 | 3% | 42,472 | 9% |
| CAPE MAY | 521 | 6% | 1,094 | 4% | 7,554 | 3% | 9,141 | 7% | 5,588 | 9% | 23,898 | 5% |
| CUMBERLAND | 30 | 0.3% | 84 | 0.3% | 417 | 0.2% | 450 | 0.3% | 331 | 1% | 1,312 | 0.3% |
| ESSEX | 989 | 11% | 2,416 | 8% | 20,809 | 9% | 15,503 | 11% | 2,136 | 4% | 41,853 | 9% |
| GLOUCESTER | 20 | 0.2% | 386 | 1% | 2,252 | 1% | 418 | 0.3% | 264 | 0.4% | 3,340 | 1% |
| HUDSON | 3 | 0.03% | 3 | 0.01% | 78 | 0.03% | 987 | 1% | 1,331 | 2% | 2,402 | 0.5% |
| HUNTERDON | 0 | 0% | 130 | 0.4% | 234 | 0.1% | 318 | 0.2% | 879 | 1% | 1,561 | 0.3% |
| MERCER | 186 | 2% | 3,722 | 12% | 40,223 | 17% | 30,575 | 22% | 10,139 | 17% | 84,845 | 18% |
| MIDDLESEX | 1394 | 15% | 2,733 | 9% | 3,627 | 2% | 4,983 | 4% | 744 | 1% | 13,481 | 3% |
| MONMOUTH | 3071 | 34% | 2,031 | 7% | 7,782 | 3% | 4,622 | 3% | 1,665 | 3% | 19,171 | 4% |
| MORRIS | 394 | 4% | 421 | 1% | 2,618 | 1% | 1,118 | 1% | 450 | 1% | 5,001 | 1% |
| OCEAN | 0 | 0% | 92 | 0.3% | 214 | 0.1% | 372 | 0.3% | 333 | 1% | 1,011 | 0.2% |
| PASSAIC | 897 | 10% | 3,530 | 12% | 58,258 | 24% | 25,361 | 18% | 13,128 | 22% | 101,174 | 21% |
| SALEM | 0 | 0% | 24 | 0.1% | 130 | 0.05% | 451 | 0.3% | 182 | 0.3% | 787 | 0.2% |
| SOMERSET | 0 | 0% | 139 | 0.5% | 1,443 | 1% | 180 | 0.1% | 109 | 0.2% | 1,871 | 0.4% |
| SUSSEX | 29 | 0.3% | 269 | 1% | 812 | 0.3% | 1,335 | 1% | 230 | 0.4% | 2,675 | 1% |
| UNION | 0 | 0% | 478 | 2% | 11,163 | 5% | 68 | 0.05% | 242 | 0.4% | 11,951 | 3% |
| WARREN | 41 | 0.5% | 141 | 0.5% | 965 | 0.4% | 7,740 | 6% | 532 | 1% | 9,419 | 2% |
| 70741 | 9, | 038 | 30, | 236 | 239, | 239,998 138,797 | | 59,000 | | | | |
| TOTAL | 2 | % | 6 | % | 50 | % | 25 | % | 12 | 2% | 477,0 | 109 |

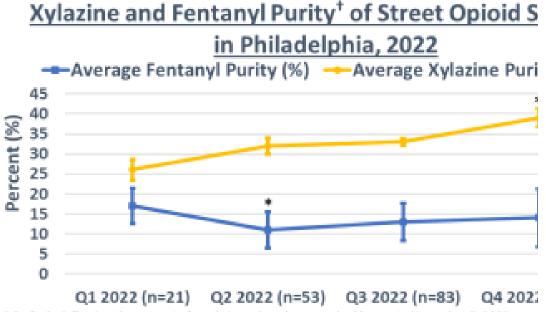
Office of Drug Monitoring & Analysis Quarterly Report







XYLAZINE EPIDEMIOLOGY



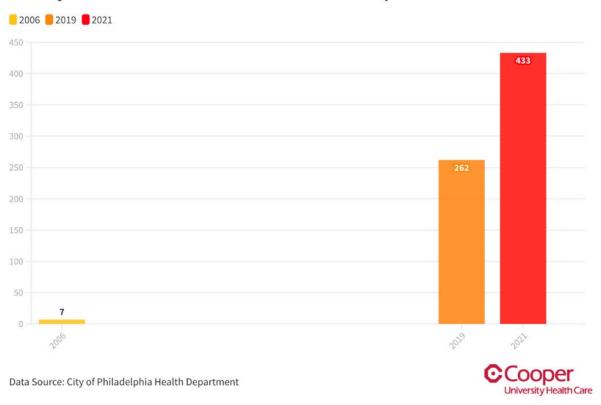
- 2021, >90% of supply in Philadelphia with
- 2022, 33% of supply in NJ with xylazine, in first quarter of 2023, up to 45%
- † Purity is defined as the amount of a substance in a drug sample; †† = up to November 5, 2022;
- * = p ≤ 0.05 (two-tailed independent samples t-test, reference group = Q1 2022).

- Contaminant first seen in early 2010s in Philadelphia/Northeast
- Spreading geographically across the nation (federal emerging health crisis)
- xylazine

Health Department Releases Data on 2021 Overdose Deaths in Philadelphia

For immediate release: October 26, 2022 | Published by: <u>Board of Health</u>, <u>Department of Public Health</u> | Contact: James Garrow <u>phlpublichealth@phila.gov</u>

2021 Xylazine-Related Overdose Deaths in Philadelphia





XYLAZINI

TABLE 2. Survey Results: Demographics, Patterns of Drug Use, and Experiences with Xylazine Demographics Age Range (n = 51) Gender (n = 51)Race (n = 50)Geography (n = 50) < 20 y8% Male 67% White, non-Hispanic 79% Northeast* 50% 20-29 y 33% Female Southeast 14% White, Hispanic 30-39 y 47% Nonbinary/other African American Midwest 14% 40-49 y 12% Southwest 0% ≥50 y 0% American Indian 4% West 10% Native Hawaiian/Pacific 12% 4% Other country? Islander Patterns of Drug Use Frequency of Xylazine Use Intentionally Seek Out to Buy Drug Use on a Typical Day Method of Xylazine Exposure Drugs That Contain (n = 60)(n = 61)(n = 61)Xylazine (n = 61)Yes Any opioids Inhalational (smoking) 20% Daily 39% 74% 57% 1-6 times per week No Fentanyl Intranasal (snorting) 19% Cannabis Injection 43% 1-4 times per month 15% Stimulants 41% Oral 3% A few times per year/rarely 27% Benzodiazepines 21% Hallucinogens 10% Experiences With Xylazine Adverse Effects From Have You Experienced What Xylazine Withdrawal How Has Withdrawing From Symptoms Have You Xylazine Use (n = 48)Withdrawal From Other Drugs Changed Since Xylazine? (n = 59)Experienced? (n = 35)You Started Using Xylazine? (n = 51)Worse Increased overdoses/passing out 81% Yes 53% Body aches 63% 57% Skin wounds or infections No Cravings The same 39% Increased emergency room visits 17% 91% Better 4% Anxiety Depressed Mood 74%



^{*}Of the 25 responses that were included from a state in the Northeast, 12 responses were from Pennsylvania.

[†]Included 2 responses from the United Kingdom, 2 responses from Canada, 1 response from Sweden, and 1 response from Ecuador.

Clonidine

Alpha adrenergic receptor agonist

Mixed mechanism of action*

- •Central alpha-2 agonist
- ↓ NE release
- JACh release
- Agonizes multiple receptors

Hypertension followed by hypotension

Respiratory depression

•Potentially lethal dose 40-2400 mg in humans

Sherri L Kacinko, Amanda L A Mohr, Barry K Logan, Edward J Barbieri, Xylazine: Pharmacology Review and Prevalence and Drug Combinations in Forensic Toxicology Casework, *Journal of Analytical Toxicology*, Volume 46, Issue 8, October 2022, Pages 911–917, https://doi.org/10.1093/jat/bkac049

XYLAZINE - PHARMACOLOGY



XYLAZINE



Created by Bayer in 1962

- Antihypertensive
- Not approved for human use trials stopped due to hypotension and sedation

Large animal sedative-analgesic

- Anestica de caballo
- "Tranq"

Comes in 20,100,300 mg/ml soln

Often used with ketamine or barbiturates

XYALZINE PHARWACOLOGY

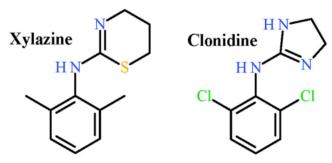


Figure 1. Chemical structures of xylazine and clonidine.

- Most common clinical side effects in humans:
- 47% drowsiness/lethargy
- 20% bradycardia
- 11% hypotension
- 9% hypertension
- 8% slurred speech

Sherri L Kacinko, Amanda L A Mohr, Barry K Logan, Edward J Barbieri, Xylazine: Pharmacology Review and Prevalence and Drug Combinations in Forensic Toxicology Casework, *Journal of Analytical Toxicology*, Volume 46, Issue 8, October 2022, Pages 911–917, https://doi.org/10.1093/jat/bkac049

XYLAZINE OVERDOSE

Opioid overdoses involving xylazine in emergency department patients: a multicenter study

Jennifer S. Love^a , Michael Levine^b, Kim Aldy^{c.d}, Jeffrey Brent^e , Alex J. Krotulski^f, Barry K. Logan^f , Carmen Vargas-Torres^a, Sara E. Walton^f, Alexandra Amaducci^a, Diane Calello^h , Robert Hendrickson^f , Adrienne Hughes^f, Anita Kurt^a, Bryan Judge^f, Anthony Pizon^f, Evan Schwarz^f , Joshua Shulman^f, Timothy Wiegand^{ff}, Paul Wax^{c.d} and Alex F. Manini^{ff}

- Multicenter study reviewing overdoses in 9 US emergency departments from 9/2022 to 8/2021
- 391 patients reviewed, 90 tested positive for xylazine
- 83% of patients received naloxone
- Xylazine-negative patients were more likely to develop a coma within 4 hours of ED arrival and suffer a cardiac arrest



Xylazine spreads across the US: A growing component of the increasingly synthetic and polysubstance overdose crisis

Joseph Friedman^{a,b,*}, Fernando Montero^c, Phillippe Bourgois^a, Rafik Wahbi^d, Daniel Dye^e, David Goodman-Meza^f, Chelsea Shover^g

Yeah accidentally. It's dangerous stuff. I was doing like zombie walks from the tranq, so I was walking, but I wasn't aware of what was going on, and I fell on the train tracks and cracked my skull. I literally cracked my skull open, and almost died. So yeah. You know, the old heroin, that was just heroin, was dangerous enough, but the tranq is just really a whole other world."

-Mike, White 40, Injects Opioids.

PATIENT EXPERIENCE OF FENTANYL AND XYLAZINE

- Fentanyl has shorter duration, faster withdrawal symptom onset, "short legs"
- Xylazine potentially adds sedative effect, making high last longer, more similar to heroin
- Risks of intense sedation



Clonidine withdrawal*

Hypertensive emergencies???

Compassionate care

*Geyskes GG, Boer P, Dorhout Mees EJ. Clonidine withdrawal. Mechanism and frequency of rebound hypertension. Br J Clin Pharmacol. 1979 Jan;7(1):55-62. doi: 10.1111/j.1365-2125.1979.tb00897.x. PMID: 760743; PMCID: PMC1429594.

Ehrman-Dupre, R., Kaigh, C., Salzman, M., Haroz, R., Peterson, L. K., & Schmidt, R. (2022). Management of xylazine withdrawal in a hospitalized patient: A case report. *Journal of Addiction Medicine*, *16*(5), 595-598.



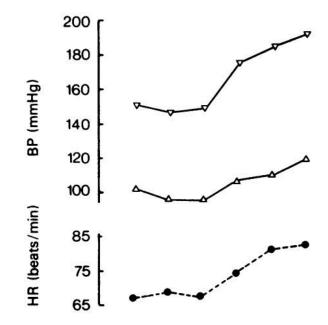


Br. J. clin. Pharmac. (1979), 7, 55-62

CLONIDINE WITHDRAWAL. MECHANISM AND FREQUENCY OF REBOUND HYPERTENSION

G.G. GEYSKES, P. BOER & E.J. DORHOUT MEES

Department of Nephrology and Hypertension University Hospital, Utrecht, The Netherlands



CLONIDINE WITHDRAWAL IN THE LITERATURE

- · Xylazine and clonidine similar in chemical structure
- Study examined 14 people with clonidine dependence and acute abruption
- 3/14 required intervention because of symptoms and increase in heart rate and blood pressure
- Increased urinary noradrenaline levels during withdrawal that peaked
- Symptoms included headache, anxiety, insomnia, palpitations and nausea



29yo female admitted to Cooper

25 bags IV fentanyl daily, knew about xylazine contaminant

Subjective differences in withdrawal from tranq dope vs. dope alone

Urine toxicology included fentanyl, tramadol, xylazine

XYLAZINE WITHDRAWAL MANAGEMENT

| | Day 1 | Day 2 | Day 3 | Day 4 | Day 5 | Day 6 |
|-------------------------------|--|--|--|--|---|---|
| Hydromorphone | Patient-controlled anesthesia (PCA) pump; settings: no basal rate, bolus 1 mg q 10 minutes | PCA pump; settings: basal rate 1 mg/ hour, bolus 1 mg q 12 minutes | PCA pump; settings: basal rate 1.5 mg/ hour, bolus 1 mg q 12 minutes | PCA pump; settings: basal rate 1.5 mg/ hour, bolus 1 mg q 12 minutes | PCA pump; settings: basal rate 1.5 mg/ hour, bolus 1.2 mg q 12 minutes | PCA pump; settings: basal rate 1.5 mg/ hour, bolus 1.2 mg q 12 minutes |
| Phenobarbital | Load (per institution's intensive care unit alcohol withdrawal protocol) | Taper (per institution's intensive care unit alcohol withdrawal protocol) | Taper (per institution's intensive care unit alcohol withdrawal protocol) | Taper (per institution's intensive care unit alcohol withdrawal protocol) | Discontinued (taper completed) | |
| Dexmeditomidine Tizanidine | Infusion 4 mg q 6 hours PO | Infusion Discontinued | Infusion | Infusion | Discontinued | |
| Clonidine | | 0.3 mg q 8 hours PO | 0.3 mg q 8 hours PO | 0.3 mg q 8 hours PO | 0.3 mg q 8 hours PO | 0.3 mg q 8 hours PO |
| Buprenorphine | | | | 300 mcg once buccal | 300 mcg BID buccal | 450 mcg BID buccal |
| Gabapentin | | | | 300 mg q 8 hours PO | 300 mg q 8 hours PO | 300 mg q 8 hours PO |
| Ketamine | | | | Infusion during dressing changes | Infusion during dressing changes | Infusion during dressing changes |

Ehrman-Dupre, R., Kaigh, C., Salzman, M., Haroz, R., Peterson, L. K., & Schmidt, R. (2022). Management of xylazine withdrawal in a hospitalized patient: A case report. *Journal of Addiction Medicine*, *16*(5), 595-598



XYLAZINE WITHDRAWAL MANAGEMENT???

| | Day 7 | Day 8 | Day 9 | Day 10 | Day 11 | Day 12 |
|---------------|---|---|--|--|--|--|
| Hydromorphone | PCA pump; settings: basal rate 1.5 mg/ hour, bolus 1.2 mg q 12 minutes | PCA pump; settings: basal rate 1 mg/ hour, bolus 1.3 mg q 12 minutes | PCA pump; settings: no basal rate, bolus 1.3 mg q 12 minutes | PCA pump; settings: no basal rate, bolus 1.3 mg q 12 minutes | PCA pump; settings: no basal rate, bolus 1.3 mg q 12 minutes | PCA pump; settings: no basal rate, bolus 1.3 mg q 12 minutes |
| Clonidine | 0.3 mg q 8 hours PO | 0.3 mg q 8 hours PO | 0.3 mg q 8 hours PO | 0.3 mg q 8 hours PO | 0.3 mg q 8 hours PO | 0.3 mg q 8 hours PO |
| Buprenorphine | 2 mg twice daily sublingual | 2 mg three times daily sublingual | 4 mg q 4 hours sublingual | 2 mg four times daily sublingual | 4 mg four times daily sublingual | 4 mg four times daily sublingual |
| Gabapentin | 300 mg q 8 hours PO | 300 mg q 8 hours PO | 300 mg q 8 hours PO | 300 mg q 8 hours PO | 300 mg q 8 hours PO | 300 mg q 8 hours PO |
| Ketamine | Infusion during dressing | Infusion during dressing | Infusion during dressing | Infusion during dressing | Infusion during dressing | Discontinued |



XYLAZINE WITHDRAWAL MANAGEMENT???

| | Day 13 | Day 14 | Day 15 | Day 16 | Day 17 | Day 18 |
|---------------|--|--|--|--|---|--|
| Hydromorphone | PCA pump; settings: no basal rate, bolus 1.3 mg q 12 minutes | PCA pump; settings: no basal rate, bolus 1.3 mg q 12 minutes | PCA pump; settings: no basal rate, bolus 1 mg q 15 minutes | PCA discontented; 2 mg q 3 hours IV PRN pain | 2 mg q 3 hours IV PRN pain | 2 mg q 4 hours PO PRN moderate pain, 2 mg q 4 hours PO PRN severe pain |
| Clonidine | 0.3 mg q 8 hours PO | 0.3 mg q 8 hours PO | 0.3 mg q 8 hours PO | 0.3 mg q 8 hours PO | 0.3 mg/24 hours transdermal patch | 0.3 mg/24 hours transdermal patch |
| Buprenorphine | 4 mg QID sublingual | 4 mg QID sublingual | 4 mg 5 times daily sublingual | 4 mg 5 times daily sublingual | 4 mg 6 times daily sublingual | 4 mg 6 times daily sublingual |
| Gabapentin | 300 mg q 8 hours PO | 300 mg q 8 hours PO | 300 mg q 8 hours PO | 300 mg q 8 hours PO | 300 mg q 8 hours PO | 300 mg q 8 hours PO |



RESULTS: XYLAZINE WITHDRAWAL SYNDROME

Major phenotypes from expert chart review:

No signs of new withdrawal syndrome: 52 of 73 (71.3%)

- Mixed opioid and benzodiazepine withdrawal
- Aggressive withdrawal & pain management

Possible withdrawal syndrome: 19 of 73 (26.4%)

- Agitated delirium/toxidrome with other substances
- Precipitated withdrawal
- Untreated opioid withdrawal

Otherwise unexplained symptoms: 2 of 73 patients (2.7%)

 Asymptomatic hypertension (~180/100s) and/or tachycardia (~90s)



RESULTS: XYLAZINE WITHDRAWAL SYNDROME

Among 73 cases with urine xylazine detected:

- High variability in patient-reported symptoms documented
- When documented, patients noted anxiety and restlessness:

"Pt is increasingly agitated & restless"

"On assessment pt tearful and anxious."

"Mood is anxious. Affect is tearful.

Behavior: Behavior is agitated"

"Pt requested PRN anxiety medication."



TABLE 2. Survey Results: Demographics, Patterns of Drug Use, and Experiences with Xylazine Demographics Age Range (n = 51) Gender (n = 51)Race (n = 50)Geography (n = 50) <20 y 8% Male 67% White, non-Hispanic 79% Northeast* 50% 20-29 y 33% Female White, Hispanic 4% Southeast 14% 30-39 y 47% Nonbinary/other 4% African American 4% Midwest 14% 40-49 y 12% Asian Southwest 0% 0% 4% West ≥50 y American Indian 10% Native Hawaiian/Pacific 4% Other country† 12% Islander Patterns of Drug Use Intentionally Seek Out to Buy Drug Use on a Typical Day Method of Xylazine Exposure Frequency of Xylazine Use Drugs That Contain (n = 60)(n = 61)(n = 61)Xylazine (n = 61)Yes 26% Any opioids Inhalational (smoking) 20% Daily 39% 74% Fentanyl No 19% Intranasal (snorting) 57% 1–6 times per week 15% Cannabis 45% Injection 43% 1-4 times per month Stimulants 41% 27% Oral 3% A few times per year/rarely 21% Benzodiazepines Hallucinogens 10% Experiences With Xylazine Have You Experienced What Xylazine Withdrawal How Has Withdrawing From Adverse Effects From Other Drugs Changed Since Xylazine Use (n = 48)Withdrawal From Symptoms Have You Xylazine? (n = 59)Experienced? (n = 35)You Started Using Xylazine? (n = 51)Increased overdoses/passing out 819 Yes 53% Body aches 63% Worse 57% Skin wounds or infections No 47% Cravings 49% The same 39% Increased emergency room visits 17% Anxiety 91% Better 4% 74% Depressed Mood

Spadaro A. J Addict Med. 2023 Nov-Dec 01;17(6):691-694. doi: 10.1097/ADM.00000000001216. Epub 2023 Aug 10. PMID: 37934533.

^{*}Of the 25 responses that were included from a state in the Northeast, 12 responses were from Pennsylvania.

[†]Included 2 responses from the United Kingdom, 2 responses from Canada, 1 response from Sweden, and 1 response from Ecuador.

XYLAZINE WITHDRAWAL SUMMARY

- Physiologically different from opioid withdrawal
- Consider higher doses of clonidine, monitor blood pressure
 - In hospital settings, other medications could be considered
- Management of opioid withdrawal symptoms also needed (full opioid agonists, methadone, buprenorphine etc)
- If patient does not know about supply contamination, consider xylazine withdrawal if symptoms not managed by traditional medications for opioid withdrawal

XYLIZINE WOUNDS

THAZINE ASSOCIATED

*photos of wounds may be disturbing

Photos from Cooper University Hospital















39 Y.O. FEMALE, LEFT ARM







PHOTOS FROM COOPER UNIVERSITY HOSPITAL



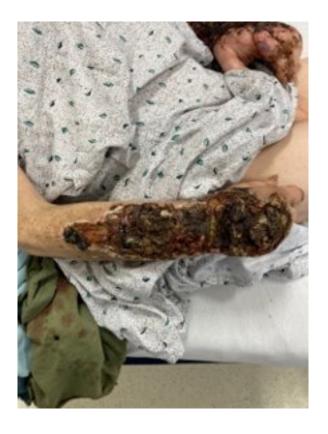


Photo courtesy of M. Coletta, MD



TABLE 1. The Prevention Point Philadelphia Wound Care Clinic's Approach to Care for Xylazine-associated Wounds

| Stepwise Dressing Change | Dressing Products Used | Notes |
|-------------------------------------|--|--|
| Step 1: Premedicate if possible | | In settings where available, advocate for adequate pain/withdrawal management before dressing change |
| Step 2: Remove soiled dressing | | Soak soiled dressing with water/saline to decrease pain with removal. Offer patient option to remove their own dressing. |
| Step 3: Clean | Normal saline, generic wound washes For wounds with heavy burden of nonviable tissue: • Vashe, Dakins 0.125% | Test cleansers on small area of wound to assess tolerance. |
| Step 4: Debride | Enzymatic debridement • Santyl: Requires prescription; costly | Topicals may be applied to the primary dressing (step 6) to avoid directly touching sensitive wounds. |
| | Autolytic: • Medihoney: Consider outdoor exposure and | Alert patient to the likelihood of increased drainage with use of topical debriding agents. |
| | potential insect attraction • Hydrogel silver • Silver gel/Silver sulfadiazine • PHMB topical | Cross-hatching of eschar, if tolerated, promotes deeper penetration of topical debriding agents and may be appropriate in some settings. |
| Step 5: Apply other topicals | Skin protectant to periwound tissue (eg no-sting skin prep, A&D ointment, Coloplast Triad) Topical antibiotic if indicated and compatible (eg, Mupirocin) | Preservation of intact periwound tissue is priority, especially with necrotic and heavily exudative wounds. Systemic antibiotics do not penetrate above the wound bed, and a topical may be required to reduce the overall bioburden. |
| Step 6: Apply primary dressing | Based on assessment of wound drainage: • Wet/normal wound: Oil-emulsion (e.g. Adaptic) • Dry wound: Petroleum-based (e.g. Xeroform) | Cut to shape of wound to avoid coverage of periwound area, which can promote breakdown. Check compatibility of Xeroform and any topicals used. |
| Step 7: Apply secondary of dressing | Super absorbent dressing, layers of woven gauze, abdominal pads, or nonstick gauze | |
| Step 8: Secure | Gauze wrap secured with Tubigrip, IV netting, self-adherent wrap, or ACE bandage | Self-adherent or ACE bandages should be applied just tight enough to secure underlying dressings, not for compression. Self-adherent wrap may contribute to skin breakdown if not changed daily. |
| Harm reduction and trauma-informe | d care considerations | |

Harm reduction and trauma-informed care considerations

- · Assess the patient's history of wound care—what dressing supplies or strategies have and have not worked?
- Ask if patient would like to remove dressing themselves, to support engagement and autonomy and minimize pain.
- Recognize the distress and stigma often associated with wound odor—offer air freshener, aromatherapy inhalers, and change trash frequently.
- Dispense oral antibiotics or other oral medications in lanyard-attached container (eg, clear plastic badge holder) to prevent theft or loss (for unhoused individuals)
- Establish a wound dressing change schedule that is feasible for patient provide dressing change supplies to accommodate several dressing changes when possible.
- Build relationships with local emergency medicine, internal medicine, infection disease and addiction medicine departments to facilitate warm handoffs of patients to and from hospitals

SURGICAL INTERVENTION?

- Not all patients are surgical candidates
- Excisional debridement should be avoided to maintain healing of the potential wound
- Stopping injecting can greatly impact healing process
 Healing process greatly slowed by ongoing injecting
- Consider operation for patients in recovery with non-healed wounds after 6 weeks of cessation

PATHOLOGY

- Injection drug use has been associated with wounds
 - •Potential causes:
 - Skin picking behavior
 - Increased frequency of injection
 - Infection
 - Compression/Pressure
 - Poor wound healing environment
 - Cytotoxic effect of drug*
 - Obliterative vasculitis from repeated injections



WOUND CARE SUPPLIES



SELF-CARE STEPS

- Clean hands with soap & water or hand sanitizer before touching wounds
- Gently wash wound with soap & water or with saline at least every 2-3 days
- Put ointment on gauze & place on entire wound. Cover with more dry gauze
- Wrap wound with kerlix and secure with medical tape. Make sure wrap is not too tight
- Cover dressing with ACE wrap or coban or with long sleeves/pants if no other option
- Change dressing every 1-3 days. Watch for red flags

XYLAZINE

// zai · luh · zeen //

AKA "Trang" or "Trang Dope"

A cutting agent making its way into the drug supply. Contamination with xylazine increases risk of sedation, overdose, and wounds that are hard to heal.

This guide focuses on xylazine wounds







Grayken Center for Addiction Training & Technical Assistance **Boston Medical Center**

XYLAZINE WOUNDS

Xylazine wounds can appear anywhere on the body regardless of where you are injecting, particularly in YELLOW areas.

Check these areas regularly for any wounds that may develop.

Wounds can occur even if you're just snorting or smoking.

RED FLAGS TO SEEK MEDICAL CARE

- Fever or chills
- · Skin turns dark or black
- Skin is red, hard, & hot to touch
- Thick, smelly yellow or green drainage
- Severe or worsening pain at wound site
- · Pain & decreased ability to move joint
- · Pieces of tissue falling off
- Exposed bone or tendon
- New numbness

Xylazine wounds can look like a combination of:

- Large ulcers Blisters
- Small scabs Eschar (dark/black pieces of dead tissue)



- Keep your skin moisturized with A+D ointment
- · Avoid using alcohol/hydrogen peroxide on wounds
- Keep wounds covered with a clean bandage
- · Wear long sleeves, pants, socks, and gloves to prevent yourself from scratching your skin
- · Eat protein & stay hydrated to help with healing
- Avoid injecting into or around your wounds
- · Use new supplies every time and avoid sharing
- · Not every wound is infected. Avoid taking nonprescribed antibiotics

Even though xylazine isn't an opioid, you should still give naloxone in an overdose as opioids are often present



NATIONAL HARM REDUCTION COALITION

XYLAZINE ONE-PAGER DRAFT (HARMREDUCTION.ORG)

XYLAZINE IN THE DRUG SUPPLY

INJECTING



Dope that's been cut with xylazine is sometimes darker, browner, chunkier, flakier, and weird-smelling. But dope that appears normal (white powder) can still have xylazine

Cooking it twice can help dissolve chunks. After drawing up, wipe off needle with an alcohol prep, let dry, THEN inject

Go as slow and precise as you can; for arms, use a tie and get the vein anchored. Count to 5 before taking the needle out. You want to avoid ANY leaking outside the vein and into the muscle or tissue

Short-tips (31g) may be higher-risk than regular 1/2" needles. Muscling and skin popping are EXTREMELY HIGH RISK for skin problems

Try booty-bumping or smoking from a hammer pipe; less injecting = less risk

WOUNDS AND WOUND CARE TIPS



Xylazine wounds can take months or years to heal, and may not heal without medical care. Wounds can get very goopy/yellow/red/swollen/tend to be most painful at this stage

If the wound goes necrotic (dead black tissue; you'll know when it happens) go to an emergency room ASAP. The first step is cleaning the wound and removing some of the dead tissue and you may need skin surgery

Can appear anywhere there's an opening in your skin — NOT just where you inject. Try to keep all cuts/wounds/injection sites clean and covered

DISCLAIMER: Advice in this guide comes from people who use xylazine or have used the tips they contributed. However, there's very little about xylazine that we know for sure, and wound progression in particular can vary widely

- The only way to know for sure whether xylazine is in your dope is through drug checking machines, which very few harm reduction programs have
- If you are part of a drug user union, harm reduction program, or health department, you can get free drug checking kits for participants through this anonymous mail-in service https://streetsafe.supply
- If you are an individual and want to test your own supply by mail, Erowid's https://DrugsData.org offers an
 anonymous service (for a fee)
- 24/7 Never Use Alone Hotline: 800-484-3731

October, 2022

FOR MORE RESOURCES, VISIT HARMREDUCTION.ORG

HARM REDUCTION COALITION



RESOURCES

- DEA: <u>The Growing Threat of Xylazine and Its Mixture</u> with Illicit Drugs (Intelligent Report)
- NIDA: Research Topics—Xylazine
- NHRC: Xylazine FAQ, Education, Webinars
- NEXT Distro: <u>Xylazine Quick Guide for People Who</u> <u>Use Drugs</u>
- NYC xylazine test strips: <u>How To Test Your Drugs</u>
 <u>Using Xylazine Test Strips (nyc.gov)</u>

Xylazine





What is Xylazine?

Xylazine is a veterinary anesthetic that's often used as a cut in street drugs. It's sometimes called tranq, tranq dope or sleep cut and people usually use xylazine unknowingly when their drugs are cut with it.

Use

For humans there isn't a prescribed use because it's intended for use in animals.

Effect:

Sedation, analgesia (pain killing like ibuprofen or advil but not opioids) and muscle relaxation. Strong sedative effects and excessive sleepiness without euphoria have been anecdotally reported to happen anywhere from 5 to 200mg.

Side Effects

Xylazine isn't intended for human use and long term use can cause skin lesions or ulcers. In high doses, respiratory depression, passing out or falling unconscious while still standing is common. Deaths are rare but have occured in humans using anywhere from 40 to 2400mg of xylazine.

Dose

There isn't an established human dose for xylazine use. For harm reduction purposes, use as little as possible if you think your drug contains xylazine. It's recommended to start as low as possible and go slow if using xylazine.

Routes of Administration

Not much is known about the human use of xylazine but there have been reports of people eating, snorting, IVing, IMing, and using xylazine subcutaneously (injection in the skin or skin-popping).

Withdrawal

Withdrawal symptoms have been reported to be mild but because of the lack of human information about xylazine your results may vary.

Withdrawal Management

Research suggests that if withdrawal symptoms are present, low dose clonidine can be used to manage withdrawal symptoms.

Overdose Prevention

Treat xylazine like you would any other drug that can cause respiratory depression such as opioids, benzos or alcohol. If combining with other drugs, keep the doses low especially if they are other depressant drugs. There isn't an overdose reversal drug for xylazine so it's recommended to not to use alone and practice harm reduction if you decide to use xylazine.



For more drug-specific information & resources, visit: www.nextdistro.org/drugspecific

www.nextdistro.org

SMS/Signal 646-389-0752 Reddit /u/nextdistro Email info@nextdistro.org

This resource is a living document that we will continue to update and refine. If you have input about how the information contained here could be improved or if you have new content to add, please email us at content @nextdistro.org.



XYLAXINE SUMMARY

- Xylazine is an alpha adrenergic agonist seen as a contaminant in fentanyl supply, increasing in prevalence across the country
- Withdrawal management can be complex
 - Think about symptoms similar to clonidine withdrawal
 - Complex management of opioid and xylazine withdrawal
- Wound bed management (similar to burn wounds?)
 - Regular dressing changes
 - Access to saline/soap and water
 - Clean dressing supplies
 - Maximize opportunities for healthy environment for skin to heal (limiting injections if possible, maximizing nutritional intake)

THANKS! QUESTIONS?

• CME info – 888-816-4893, 19110





Bruce Ruck, Pharm.D., DABAT

Managing Director and Director of Drug Information

and Professional Education

New Jersey Poison Information and Education System







Bruce Ruck, Pharm.D., DABAT 1-800-222-1222 Managing Director & Director of Drug Information and Professional Education

New Jersey Poison Information and Education System



NJPIES



- Regionally certified Poison & Drug Information Center
 - ~ 50,000 calls a year for assistance
 - 800 222 1222

AIDS STD hotline 800 624 2377

COVID Hotline 800 962 1253 (since Jan 2020)





NJPIES

 Staffed by physicians, nurses and pharmacists

24/7

 Specially trained in toxicology and Drug Information





NJPIES-Initial Cases

47 yo found unresponsive with a bottle of alprazolam and Neptune's Fix.

 26 yo brought into ED by relative who found him with altered mentation/not responding after ingestion of Neptune's Fix which he used for abuse purposes. Relative also thought it contained Kratom, which was not listed on the label.





NJPIES-Initial Cases

 47 yr old brought into ED by EMS after being found lethargic at home. Received naloxone and woke up. Family said he took Neptune's Fix elixir. He was seen a week or so prior for a similar situation. He remained lethargic for several hours.

 69yo brought into the ED after family found him with altered mental status. They found an empty bottle of "Neptune's Fix Elixir -Tianeptine" on his nightstand. RN mentioned patient was in the ICU yesterday with the same presentation - code stroke was called but was negative -- and patient signed out AMA yesterday





Tianeptine

- Atypical antidepressant structurally similar to tricyclic antidepressants
 - enhancement of serotonin reuptake
 - agonism at the mu opioid receptor
 - reports of overdoses leading to naloxone-responsive respiratory depression
 - reports of opioid like withdrawal upon cessation of chronic use
- Approved for use in Europe, Asia, and Latin America





NJPIES-Initial action

- August 21st, NJPIES alerted NJDOH and DOC about a cluster of tianeptine exposures.
- From June 17th to Aug 17th, 2023, we received 9 exposure calls from healthcare facilities.
 - As of 2/19- 38 cases in 35 unique patients
- We provided information from our cases, the literature, as well as an FDA warning that was issued in 2022 about Tianeptine.
 - https://www.fda.gov/consumers/consumer-updates/tianeptine-products-linkedserious-harm-overdoses-death
- We increased our vigilance in keeping track of cases
 - Obtained product from those that still had bottles, we purchased some bottles, and asked hospitals to send out blood for analysis.





NJDOH-Initial action

- DOH prepared an alert based upon our report
- Alert was distributed ~ 8/25/2023



Health Alert: Tianeptine or "Gas Station Heroin"

Background

The New Jersey Poison Center (NJPIES) has recently identified a cluster of poisoning cases involving tianeptine, a substance with opioid-like effects that is being falsely marketed and sold across the state in gas stations and online as a dietary supplement. Common names for tianeptine include "gas station heroin," "ZaZa Red," or "Neptune's Elixir" (among others). Tianeptine use can lead to serious health complications and even death.

Over the 60-day period from June 17 to August 17, NJPIES has received 9 calls about patients poisoned by tianeptine, and some patients have become critically ill. Due to this cluster of cases and previous <u>FDA warnings</u>, the NJDOH has increased surveillance efforts around this substance and urges New Jersey residents to be cautious.

What is Tianeptine?

Tianeptine is a tricyclic antidepressant used in some Latin American, Asian, and European countries but is not FDA approved or regulated for use in the United States. Individuals with an opioid use disorder may be more likely to use tianeptine, as it is inaccurately marketed as a safer alternative to opioids and can have opioid-like effects. The FDA has warned that manufacturers of tianeptine are making inaccurate and unproven claims that use of tianeptine can improve brain function, treat anxiety, depression, pain, opioid use disorder, and other health ailments.



Image courtesy of Appalachia High Intensity Drug Trafficking Area (AHIDTA)





Neptune's Fix









Tianeptine

- Use and abuse of tianeptine has been around for many years
 - the cluster in NJ ignited our interest and concern
- MMWR 2018 described 218 calls to poison centers from 2000-2017
 - including reports of acute intoxication, withdrawal, and co-ingestions.
 - Majority of cases were from 2015-2017
- Rushton et al in 2021 reported 48 calls to poison centers from 2015-2020,
 - 37 of those cases from 2019-2020.
- MMWR Feb 2024, Cluster of Severe Illness from Neptune's Fix Tianeptine Linked to Synthetic Cannabinoids — New Jersey, June–November 2023
 - Based upon NJPIES data





Analytical testing of Tianeptine from NJ samples

| Sample | Sample Analysis | |
|------------------------------|--------------------|--|
| | Kavain | |
| Neptune's Fix, open bottle | Tianeptine | |
| | | |
| | MDMB-4en-PINACA | |
| | ADB-4en-PINACA | |
| | CBD | |
| | THC | |
| Neptune's Fix, closed bottle | Tianeptine | |
| | | |
| Neptune's Fix, open bottle | Kavain, Tianeptine | |

| Sample | Sample Analysis |
|----------------------------|-----------------|
| | |
| | MDMB-4en-PINACA |
| | ADB-4en-PINACA |
| | CBD |
| | THC |
| Neptune's Fix, open bottle | Tianeptine |
| | Kavain |
| Neptune's Fix, open bottle | Tianeptine |
| | Kavain |
| Neptune's Fix, open bottle | Tianeptine |





Analytical testing of Tianeptine

- Kavain
 - the main kavalactone found mostly in the roots of the kava plant
- MDMB-4en-PINACA
 - common synthetic cannabinoid identified by the Drug Enforcement Administration
 - acts as a potent agonist of the CB₁ receptor
 - has been found in samples of heroin, fentanyl, etc
 - DEA had it placed in <u>schedule I status</u> starting on December 12, 2023 for up to 2 years, they can file for permanent scheduling within those 2 years

ADB-4en-PINACA

- synthetic cannabinoid
- DEA had it placed in <u>schedule I status</u> starting on December 12, 2023 for up to 2 years, they
 can file for permanent scheduling within those 2 years

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New Jersey Medical School



Analytical testing of Tianeptine in blood samples

| Sample | Sample Analysis | |
|--------|----------------------------|--|
| | Tianeptine 460 ng/mL | |
| | MBMB-4en-PINACA | |
| Blood | detected | |
| | | |
| | Tianeptine 89 ng/ml | |
| | | |
| | Synthetic cannabinoids not | |
| Blood | detected | |





Whack a Mole

2023-2024



2017-2018







NJPIES- Withdrawal

- 27 yo male presented to the ED requesting assistance with stopping tianeptine and entering rehab. Reported taking 7g/day and has weaned himself down to 1g/day. Was admitted for inpatient detoxification.
- 32 yo male developed withdrawal symptoms after stopping Neptune's Fix tablets. Symptoms began 12 hours after the last dose, and he presented to the ED with body aches, piloerection, vomiting, diarrhea, and dilated pupils. He reported taking 90 tablets of Neptune's Fix tablets per day. Symptoms improved with buprenorphine and clonidine.





NJPIES-Demographics and Clinical Characteristics

| Median age (range) — yr | 38 (19-69) |
|-------------------------|------------|
| Sex — no. (%) | |
| Male* | (74%) |
| Female | (26%) |



^{*} Several had more than one ED visit/hospital admission



NJPIES- Clinical Characteristics

| Tachycardia | 19(56%) |
|----------------------------|------------|
| Hypotension | 13(38.25) |
| QRS Prolongation > 100 ms | 7(20.59%) |
| QTc Prolongation >= 480 ms | 9(26.47%) |
| Altered mental status | (100%) |
| Respiratory Depression | 13(38.24%) |
| Seizure | 14(42%) |
| Tremor | 4(11.76%) |
| Agitation | 8(23.5%) |
| Mydriasis | 6(17.6%) |
| Urinary Retention | 3(8.82%) |
| Cardiac arrest | 1(2.94%) |
| | |

| Acute kidney injury (Cr >1.3) | 6(17.7%) |
|-------------------------------|----------|
| Hypokalemia (<3.5) | 6(17.7%) |
| Acidosis (pH <7.3) | 5(14.7%) |





NJPIES- Therapies and Disposition

| Mechanical ventilation | 14(41.2%) |
|------------------------|-----------|
| | |
| Benzodiazepines | 18(52.9%) |
| Antipsychotics | 4(11.8%) |
| | |
| Naloxone | 11(32.5%) |

| Discharged from ED * | 8(23%) |
|-----------------------------|---------|
| Admitted to Floor * | 2(5.9%) |
| | |
| Admitted to Critical Care * | 22(64%) |

^{*} Final disposition of several cases not confirmed





NJPIES- Where was product obtained

| Gas Station | 15 |
|------------------|----|
| Convivence store | 3 |
| Vape/smoke shop | 3 |
| Online | 1 |
| Deli | 1 |
| Unknown | 12 |





NJPIES- Where were patients located

| County | No | % |
|------------|----|-------|
| Monmouth | 9 | 25.71 |
| Middlesex | 7 | 20 |
| Ocean | 5 | 14.29 |
| Atlantic | 3 | 8.57 |
| Camden | 3 | 8.57 |
| Hudson | 2 | 5.71 |
| Morris | 2 | 5.71 |
| Burlington | 1 | 2.86 |
| Mercer | 1 | 2.86 |
| Salem | 1 | 2.86 |
| Somerset | 1 | 2.86 |





Legal status

- Banned or restricted in at least 9 states
 - Florida
 - Alabama
 - Georgia
 - Indiana
 - Kentucky
 - Michigan
 - Mississippi
 - Ohio
 - Tennessee





Recalled Nep

- 1/23/24 Neptune Resources, LLC, agrees to recall Neptune's Fix products nationwide due to serious health risks
- 2/15/2024 Super Chill Products, agrees to recall their Neptune's Fix product



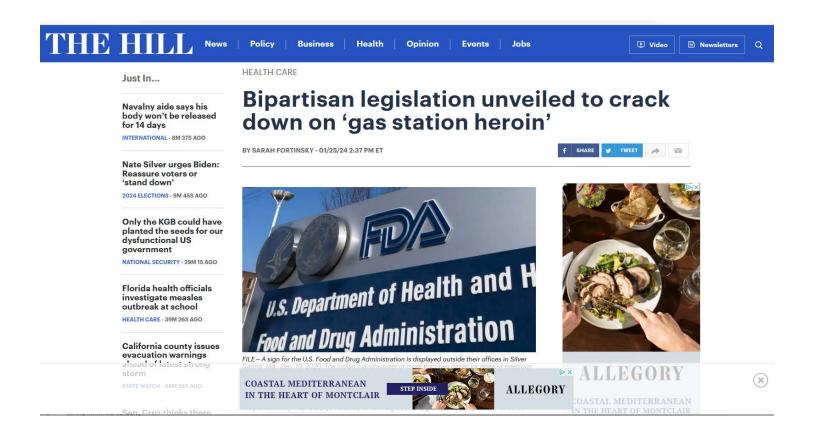








Federal status







January 2024

Results for NJ legislative search about tianeptine

Showing records 1 - 1 of about 1 results (0.001 seconds)









- Fdit Search Parameters

Create Search Alert

| Match | State | Bill | Status | Summary/Title | Last Action▼ |
|-------|-------|------|--------------|--|---|
| 100% | NJ | S729 | Intro 25% | Establishes tianeptine as Schedule II controlled dangerous substance. [Detail] [Text] [Discuss] | 2024-01-09 To Senate Judiciary Committee |



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New Jersey Poison Information & Education System

Help is a phone call away



Questions?













To register for continuing education for today's webinar, visit knockoutday.drugfreenj.org/feb29

For 1.0 EMT CEU, visit KnockOutDay.DrugFreeNJ.org/EMT

UPCOMING WEBINAR

When Addiction & Mental Health Collide 11 a.m. Thursday, March 28, 2024 Register at KnockOutDay.DrugFreeNJ.org/events

