

2023 Naloxone Update

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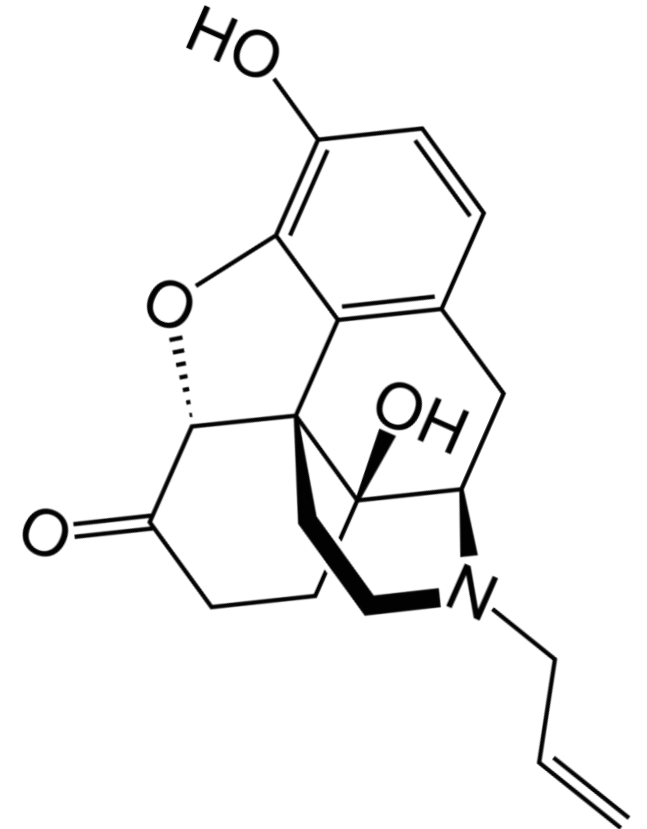
Kentucky Pharmacy Education & Research Foundation

Objectives

- Learn a brief history of naloxone as well as the currently available formulations, including OTC
- Learn about the opioid antagonist nalmefene
- Be able to dispel some myths regarding fentanyl
- Understand what fentanyl strips are and how they work as a harm reduction tool
- Learn about changes to 201 KAR 2:360 and how it might be used to help your institution distribute more naloxone to high-risk individuals
- Learn about the Kentucky Naloxone Copay Program and how your institution might be able to use it to assist your patients.

Naloxone

- Patented in 1961 and first approved for use in humans in 1971
- Naloxone is a non-selective, competitive opioid receptor antagonist
- Mean serum half life is 30-81 minutes
- No known maximum dose
- No known drug interactions
- No known disease interactions
- **Usually takes at least *1-2 minutes* or longer to begin working**



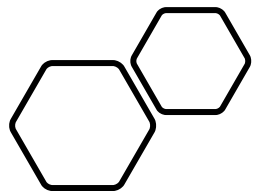
Naloxone 0.4mg and 2mg/2ml injection



- Historically available as either a 0.4mg / ml IM/IV injection vial or ampoule as well as a 2mg / 2ml prefilled IM/IV syringe

- In the mid 2000s a mucosal atomization device was developed to provide the first (non-FDA approved) nasal delivery mechanism for naloxone. The atomizer was attached to the prefilled syringe using the Luer Lock system.





NARCAN[®] 4mg (naloxone HCL) Nasal Spray



- First FDA approved nasal delivery formulation of naloxone in 2015
- Packaged as two (2) single dose nasal sprays.
- Multiple generic formulations of the 4mg nasal spray now available.
- Approved to go over the counter (OTC) in the spring of 2023 and is currently available OTC at retail locations everywhere.



NARCAN[®] 4mg OTC (naloxone HCL) Nasal Spray



- Same formulation as Rx Narcan
- Rx Narcan no longer available, however it will be found in circulation
- KY Medicaid is still covering the OTC formulation for patients once per month at no cost.
- OTC formulation is covered under the KY State Naloxone Prescription Copay Program
- ***MSRP is \$44.99 (May see locally higher prices)***
- At least one generic OTC product has been approved and will arrive by Q1 24

NARCAN[®] Storage and Handling

- Store NARCAN[®] at room temperature between 59°F to 77°F (or for short periods of time between 39°F to 104°F).
- It is best practice to not freeze NARCAN[®], however the manufacturer has frozen and thawed it multiple times in testing and the product is still effective.
- Keep NARCAN[®] in its box until ready to use and protect from sunlight.
- Replace NARCAN[®] before the expiration date on the box.

https://www.accessdata.fda.gov/drugsatfda_docs/label/2015/208411bl.pdf

<https://www.narcan.com/frequently-asked-questions>

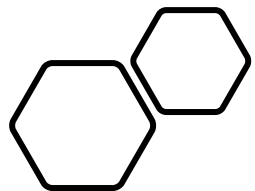
NARCAN® Info and Safety Considerations

- NARCAN® is safe to use in infants, children, adults and seniors as well as pets.
- A patient does not have to be breathing for NARCAN® to work.
- No known drug interactions.
- No significant side effect profile
 - Dizziness
 - Tiredness
 - Flushing
 - Irritability
- Side effects may be related to withdrawal of opioids from the system as opposed to the NARCAN® itself.

RiVive™ Naloxone Nasal Spray 3mg



- Produced by Harm Reduction Therapeutics (HRT), a 501(c)(3) nonprofit pharmaceutical company.
- HRT aims to provide nasal naloxone as close to manufacturer cost as possible with a stated goal that:
 - “No company, entity, or individual will profit from sales of RiVive™”
- No plans at this time to make available via retail outlets.
- Per HRT, price will be \$36 per two-dose unit
- Should be available Q4 2023 or Q1 2024



KLOXXADO[®] (naloxone HCl) 8 mg Nasal Spray

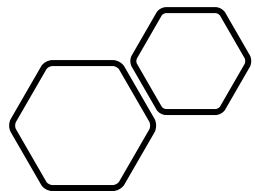


- KLOXXADO[®] was the first “high” dose naloxone product on the market with 8 mg of naloxone compared to 4 mg in NARCAN[®]
- KLOXXADO[®] is administered nasally exactly the same way as NARCAN[®]



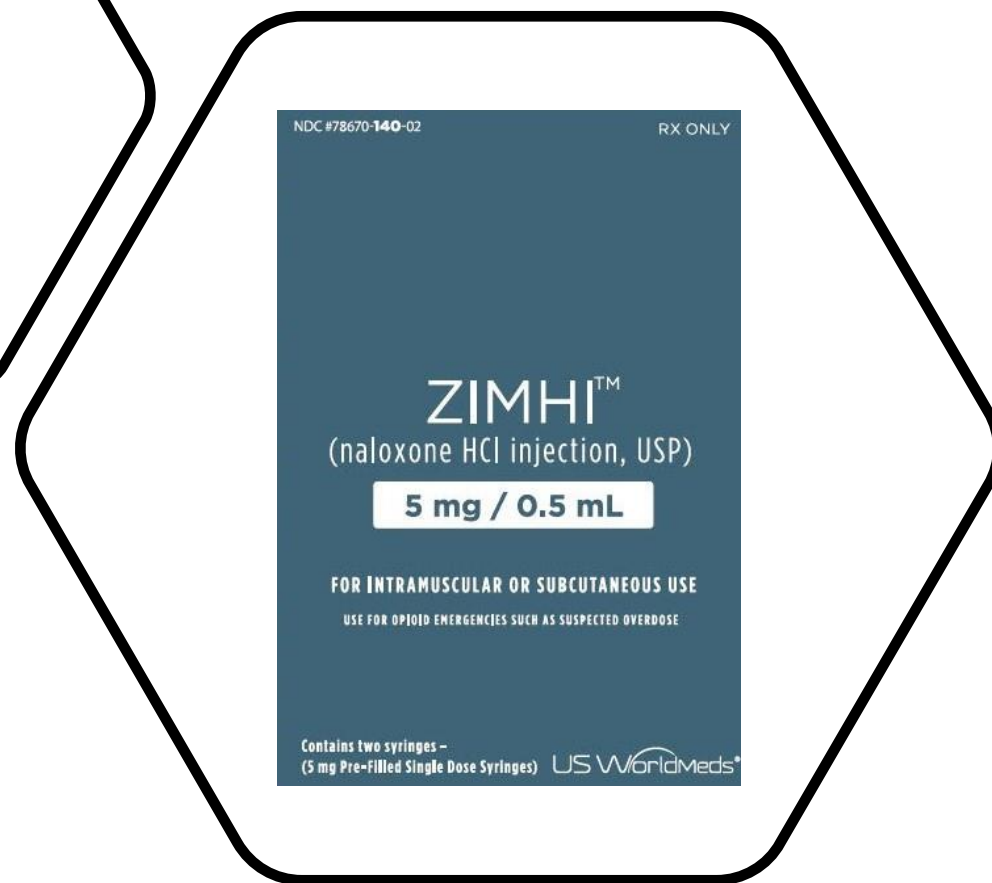
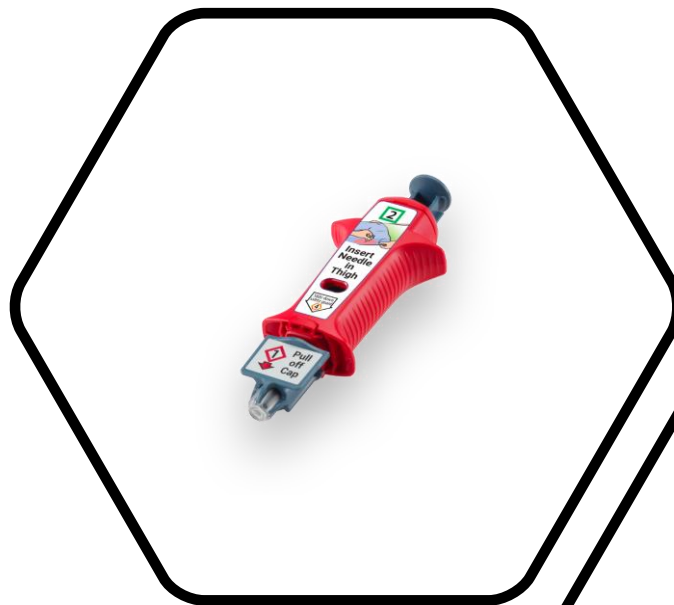
KLOXXADO® Storage and Handling

- Store KLOXXADO® at room temperature between 59°F to 77°F
- KLOXXADO® may be stored for short periods between 39°F to 104°F . Do not store above 104°F
- Do not freeze KLOXXADO®
- Keep KLOXXADO® in its box until ready to use. Protect from light.
- Replace KLOXXADO® before the expiration date on the box.



ZIMHI[®] (naloxone HCl injection)

- ZIMHI[®] is naloxone in a prefilled syringe for intramuscular injection.
- ZIMHI[®] offers the highest available dose of naloxone at 5 mg/ 0.5 mL



ZIMHI® Administration



PRESS

PRESS needle into outer thigh after twisting off needle cap



PUSH

PUSH plunger to inject until it clicks and hold for 2 seconds before removing needle



PULL

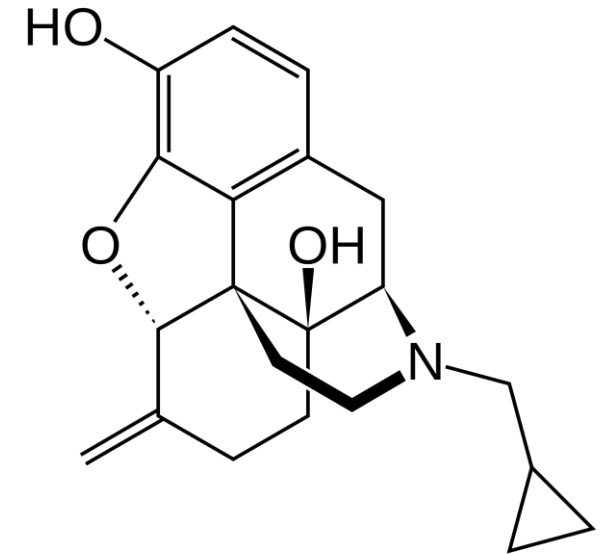
PULL the safety guard over the needle using one hand, with fingers behind the needle

ZIMHI[®] Storage and Handling

- Store ZIMHI in the outer case provided
- Store at controlled room temperature 68°F to 77°
- Do not refrigerate
- Protect from light, extreme heat, and freezing
- Prior to a medical emergency (during storage), periodically visually inspect ZIMHI through the viewing window on the device. If the solution is a yellow or brown color, cloudy, or contains particles, replace ZIMHI

Nalmefene

- Derivative of naltrexone, first reported in 1975
- Nalmefene is an opioid antagonist (like naloxone) used for the reversal of opioid drug effects
- First approved as an injectable product in 1995 and sold under the brand Revex. This product was discontinued by the manufacturer around 2008
- February 2022 the FDA approved Purdue Pharma's Nalmefene hydrochloride injection for medical use
- Serum half life of nearly 11 hours with the ability to reverse opioid intoxication for up to 8 hours



https://www.accessdata.fda.gov/drugsatfda_docs/label/2006/020459s006lbl.pdf
<https://www.fda.gov/news-events/press-announcements/fda-approves-prescription-nasal-spray-reverse-opioid-overdose>

Opvee® Nalmefene Nasal Spray 2.7mg



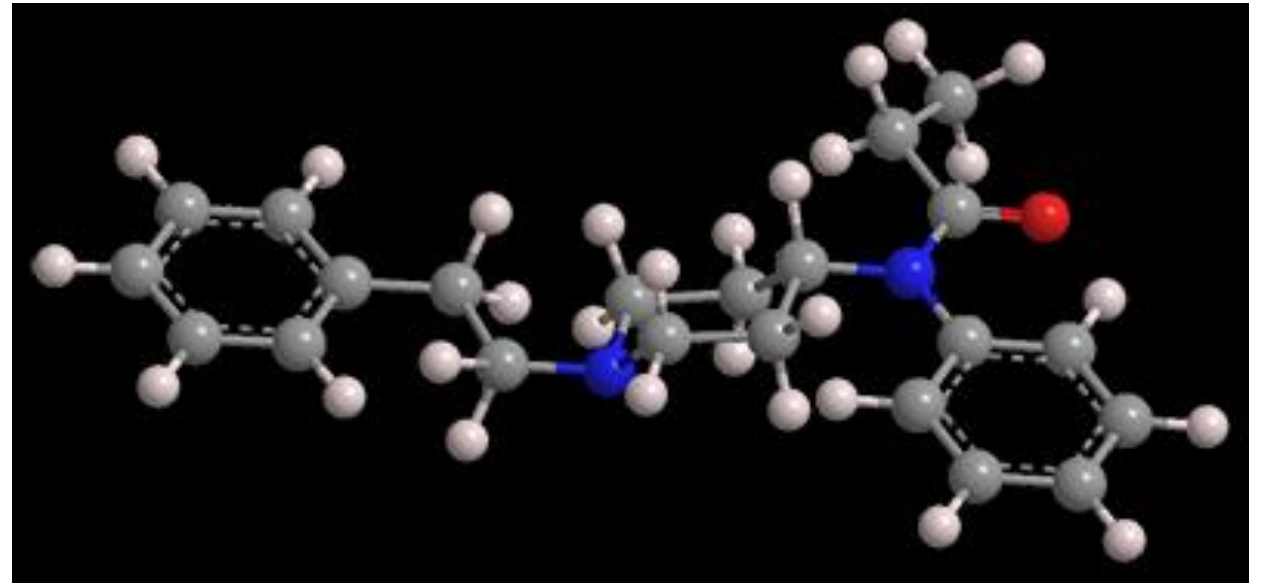
- On May 22, 2023, the FDA approved prescription nalmefene in a nasal delivery device similar to naloxone.
- Opvee® 2.7mg / 0.1ml nasal spray will be available in Q4 of 2023 or Q1 of 2024.

Nalmefene Safety Considerations

- The most common adverse reactions reported with nalmefene injection were nausea, vomiting, tachycardia, hypertension , postoperative pain, fever, and dizziness
- Nalmefene, like all opioid antagonists, can cause acute withdrawal symptoms
- Nalmefene is contraindicated in patients with known hypersensitivities to the product

What is fentanyl?

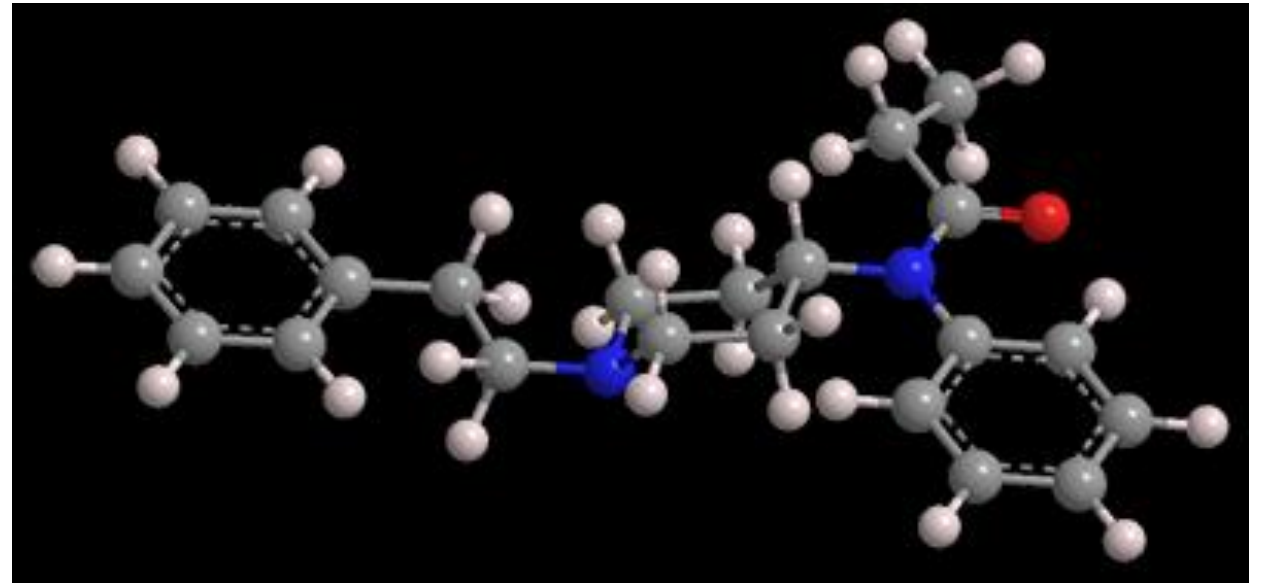
- Fentanyl is a potent synthetic opioid.
 - It is up to 50 times stronger than heroin and 100 times stronger than morphine.



American Chemical Society

What is fentanyl?

- There are two types:
 - Pharmaceutical fentanyl
 - Unregulated fentanyl



American Chemical Society

What is fentanyl?

- Pharmaceutical fentanyl
 - Generic
 - Sublimaze®
 - Duragesic®
 - Actiq®



MMM – Medical, Marketing, & Media



Drugs.com



Pfizer Hospital US



MDSupplies

What is fentanyl?

- Fentanyl is routinely administered in hospitals and by EMS to treat pain.
 - The usual starting dose is 50-100 micrograms or 0.05-0.1 milligrams.
 - The estimated lethal dose of fentanyl for a person with no tolerance is 2 milligrams (2000 micrograms) administered intravenously.



MMM – Medical, Marketing, & Media



Drugs.com



Pfizer Hospital US



MDSupplies

What is fentanyl?

- Unregulated fentanyl
 - includes fentanyl and fentanyl analogs
 - and is found in many different forms.



RTI International



The Wall Street Journal



DEA



DEA

What is unregulated fentanyl?

- In powdered form, it looks like many other drugs.
 - Unregulated fentanyl may be added to
 - heroin
 - methamphetamine
 - cocaine



RTI International



The Wall Street Journal



DEA



DEA

What is unregulated fentanyl?

- Unregulated fentanyl may be pressed into counterfeit pills that look like
 - prescription opioids
 - generic oxycodone
 - M-30s
 - benzodiazepines
 - Xanax



RTI International



The Wall Street Journal



DEA



DEA

What is unregulated fentanyl?

- It is impossible to tell if a substance contains fentanyl by appearance, taste, or smell.
- Fentanyl test strips are the best way to detect fentanyl outside of a laboratory.



Stephen Crocker/Brown University

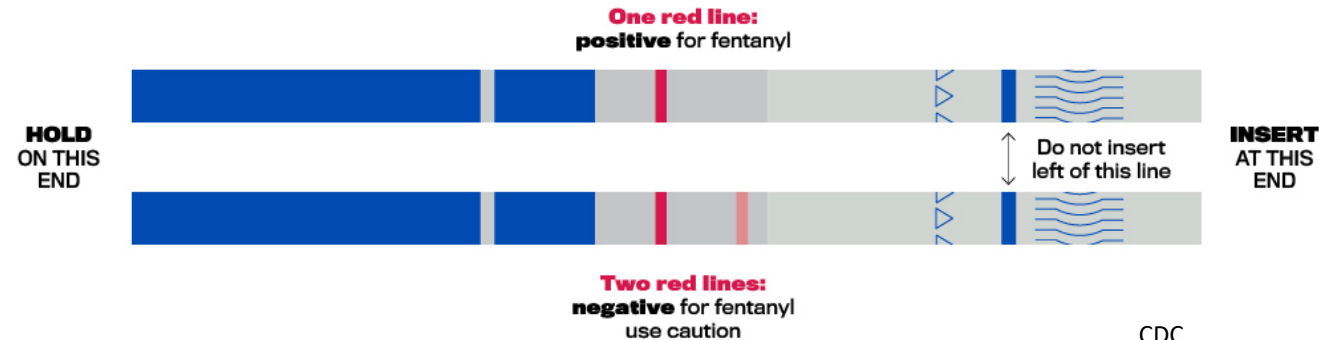


What are fentanyl test strips?

- Fentanyl test strips (FTS) can detect the presence of fentanyl in powders and pills.
 - FTS work quickly - results typically appear in five minutes.
 - FTS may not detect all fentanyl analogs.
 - FTS do not detect non-opioids such as xylazine.
 - A positive result is an opportunity for a person who uses drugs to avoid or use less of that substance.



Stephen Crocker/Brown University



What are fentanyl test strips?

- In 2023, KY House Bill 353 was passed
- Prior to passage, fentanyl test strips were considered drug paraphernalia and thus illegal to possess or use.
- House Bill 353 decriminalized fentanyl test strips and they are now available to purchase online and have shipped to Kentucky residents.
- Many local health departments and harm reduction organizations are also making them available to individuals that use drugs.

Fentanyl can be deadly to people who use drugs.

- When people use drugs, they specifically choose routes of administration to ensure that the substances enter the blood and brain.
 - People using fentanyl overdose when they are intentionally
 - injecting,
 - snorting,
 - or smoking fentanyl,
 - but *not* routinely when handling or preparing the drug.



mckesson.com



filtermag.org



KUOW.org

Fentanyl is extremely unlikely to harm people who do not use drugs.



J Med Toxicol. 2017 Dec; 13(4): 347-351. PMCID: PMC5711758
Published online 2017 Aug 25. doi: [10.1007/s13181-017-0628-2](https://doi.org/10.1007/s13181-017-0628-2) PMID: [28842825](https://pubmed.ncbi.nlm.nih.gov/28842825/)

ACMT and AACT Position Statement: Preventing Occupational Fentanyl and Fentanyl Analog Exposure to Emergency Responders

Michael J. Moss,¹ Brandon J. Warrick,² Lewis S. Nelson,³ Charles A. McKay,⁴ Pierre-André Dubé,⁵ Sophie Gosselin,⁶ Robert B. Palmer,⁷ and Andrew I. Stolbach^{2,8}

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The position of the American College of Medical Toxicology (ACMT) and American Academy of Clinical Toxicology (AACT), is as follows:

Fentanyl and its analogs are potent opioid receptor agonists, but the risk of clinically significant exposure to emergency responders is extremely low. To date, we have not seen reports of emergency responders developing signs or symptoms consistent with opioid toxicity from incidental contact with opioids. Incidental dermal absorption is unlikely to cause opioid toxicity. For routine handling of drug, nitrile gloves provide sufficient dermal protection. In exceptional circumstances where there are drug particles or droplets suspended in the air, an N95 respirator provides sufficient protection. Workers who may encounter fentanyl or fentanyl analogs should be trained to recognize the signs and symptoms of opioid intoxication, have naloxone readily available, and be trained to administer naloxone and provide active medical assistance. In the unlikely event of poisoning, naloxone should be administered to those with objective signs of hypoventilation or a depressed level of consciousness, and not for vague concerns such as dizziness or anxiety. In the absence of prolonged hypoxia, no persistent effects are expected following fentanyl or fentanyl analog exposures. Those with small subclinical exposures and those who awaken normally following naloxone administration will not experience long-term effects. While individual practitioners may differ, these are the positions of American College of Medical Toxicology and American Academy of Clinical Toxicology at the time written, after a review of the issue and scientific literature.

In 2018, The American College of Medical Toxicology (ACMT) and American Academy of Clinical Toxicology (AACT) released a [position paper](#) stating that

“the risk of clinically significant exposure to emergency responders is extremely low.”

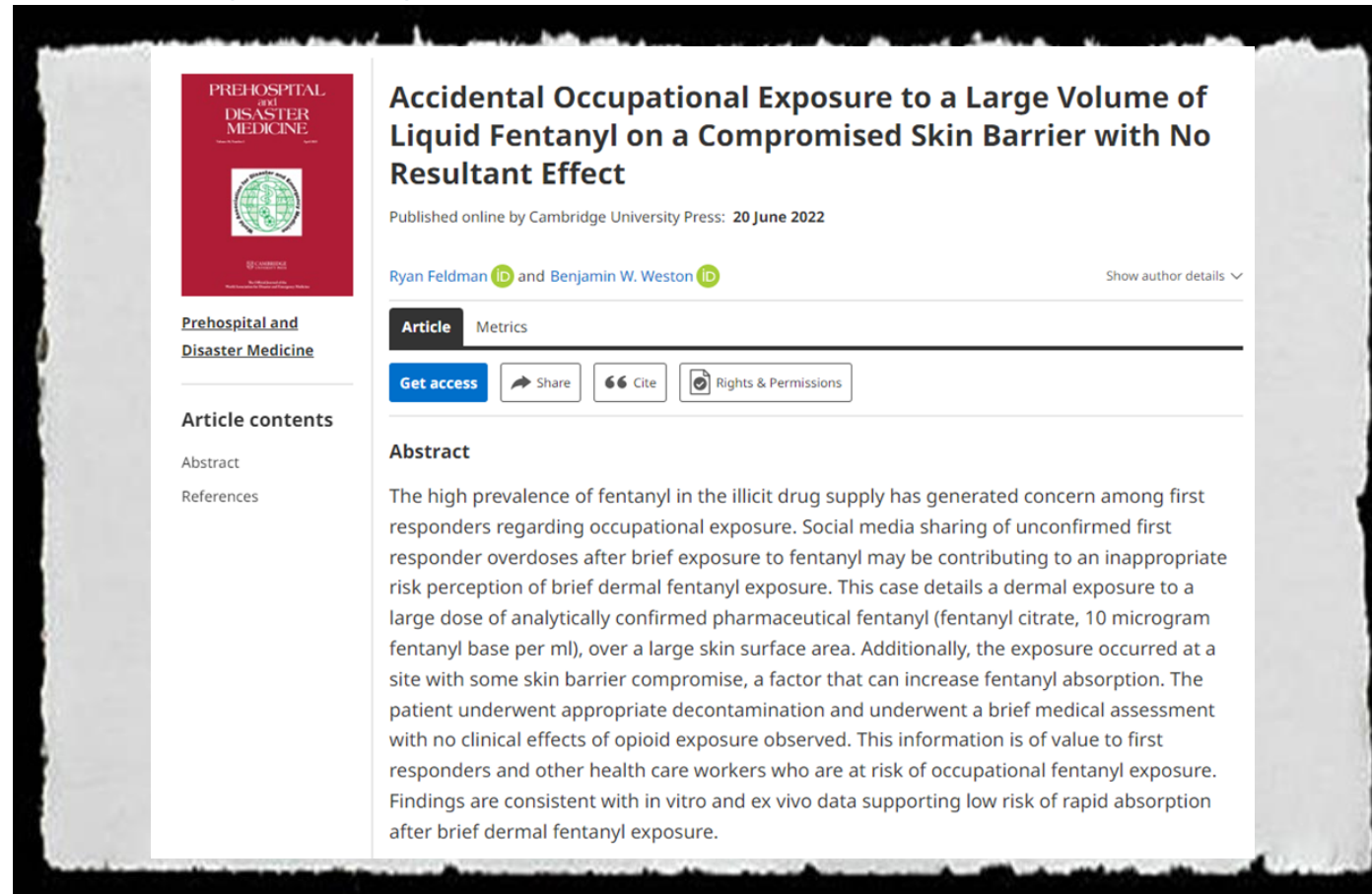
Fentanyl is extremely unlikely to harm people who do not use drugs.



Skin absorption is
“unlikely to cause toxicity.”

- If a person covered both palms with fentanyl patches it would take 14 minutes for that person to receive 100 micrograms of fentanyl.
- This is just 1/20th of the lethal dose of 2 mg.

Fentanyl is extremely unlikely to harm people who do not use drugs.



The image shows a screenshot of a research article page. On the left is a red sidebar with the journal logo and navigation links. The main content area features the article title, authors, and an abstract. The article title is "Accidental Occupational Exposure to a Large Volume of Liquid Fentanyl on a Compromised Skin Barrier with No Resultant Effect". The authors are Ryan Feldman and Benjamin W. Weston. The abstract discusses the high prevalence of fentanyl in the illicit drug supply and the concern among first responders regarding occupational exposure. It details a case of dermal exposure to a large dose of analytically confirmed pharmaceutical fentanyl (fentanyl citrate, 10 microgram fentanyl base per ml) over a large skin surface area. The patient underwent appropriate decontamination and a brief medical assessment with no clinical effects of opioid exposure observed. The findings are consistent with in vitro and ex vivo data supporting low risk of rapid absorption after brief dermal fentanyl exposure.

View the paper [HERE](#).

Fentanyl is extremely unlikely to harm people who do not use drugs.

Inhalation can cause exposure if drug particles are suspended in the air.

This unlikely to occur

through casual contact

with a person who has overdosed,

but *can* happen

in factories where fentanyl is produced.

- In this situation over three hours of exposure is required for a person to receive 100 micrograms of fentanyl – 1/20th of a lethal dose.



12 WBOY

Lewis County Sheriff's Office warns of fentanyl hidden in dollar bills

by Sam Kirk
Posted: Jul 14, 2022 / 04:36 PM EDT
Updated: Jul 14, 2022 / 04:36 PM EDT

NEWS

CA teen arrested for bringing fentanyl to school, causing employee to overdose

By Michael Lee, Fox News

September 11, 2022 | 3:54pm | Updated

41 Comments

PUBLIC SAFETY

'I'm not going to let you die': Deputy collapses after handling suspected fentanyl

The San Diego Union-Tribune

WSMV4

News First Alert Weather Watch Live Submit Photos & Video As Seen on WSMV

Flood Advisory Is In Effect

Woman hospitalized after touching dollar bill she believes contained fentanyl

News Channel 8

VIDEO: Florida cop treated for overdose after possible fentanyl exposure, police say

by Athina Morris
Posted: Dec 14, 2022 / 09:43 AM EST
Updated: Dec 15, 2022 / 05:20 AM EST

CBS NEWS

Tennessee officials warn of potential danger of fentanyl-laced dollar bills

BY TORI B. POWELL
UPDATED ON: JUNE 14, 2022 / 5:05 PM / CBS NEWS

NEW HAMPSHIRE

Officer Recalls Falling Ill to Fentanyl Exposure

By Katherine Underwood • Published June 15, 2017 • Updated on June 15, 2017 at 6:17 pm

10 BOSTON LOCAL WEATHER INVESTIGATIONS VIDEOS SPORTS U.S. & WORLD TRAFFIC NEWSLETTERS

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BILLERICA

BillERICA Officer Hospitalized After Fentanyl Exposure – But Experts Say It Probably Wasn't an Overdose

There have been numerous reports in recent years of first responders "overdosing" after coming in contact with unknown powdered substances, but medical experts say a brief exposure would not typically be dangerous

By Bianca Beltrán • Published April 21, 2023 • Updated on April 21, 2023 at 7:05 pm

The New York Times

Video of Officer's Collapse After Handling Powder Draws Skepticism

Medical experts said the video promoted a false narrative and confusion about fentanyl and ways it can lead to an overdose.

KTVB 7 News Weather Sports VERIFY KTVB 7+

THE 208

'You cannot give yourself Narcan if you are experiencing a fentanyl overdose': Specialists weigh in on a Caldwell officer overdose

Police said an officer overdosed on fentanyl. Expert said, "definitively, is that in this story, and every other story like this, this is not a fentanyl overdose."

SHARE & SAVE — f t e ...

NBC NEWS

Viral video of San Diego deputy's fentanyl exposure raises questions

U.S. NEWS

Viral video of San Diego deputy's fentanyl exposure raises questions

Some experts expressed doubts about the scenario. "You can't just touch fentanyl and overdose," physician Ryan Marino said.

LOUISVILLE PUBLIC MEDIA

NEWSLETTERS SIGN IN NPR SHOP

NEWS CULTURE MUSIC PODCASTS & SHOWS SEARCH

HEALTH

Cops say they're being poisoned by fentanyl. Experts say the risk is 'extremely low'

May 16, 2023 • 6:15 PM ET
Heard on All Things Considered
By Brian Mann

201 KAR 002:030, 201 KAR 002:360 and 201 KAR 002:460

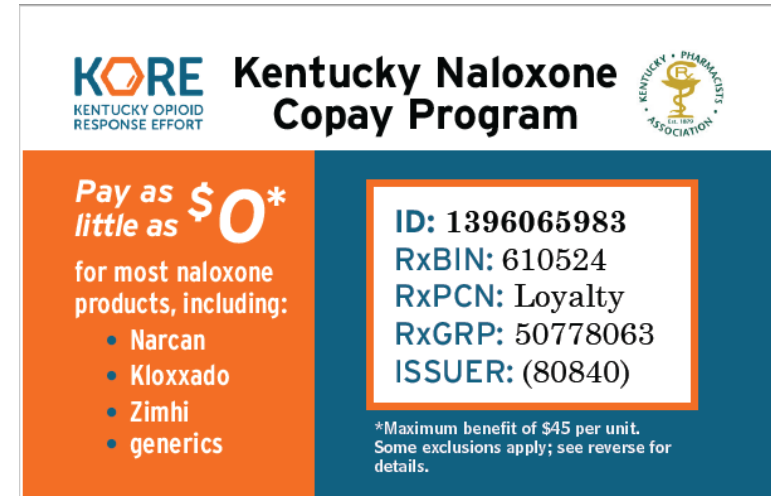
- March of 2023, the Kentucky Board of Pharmacy approved an amendment to 201 KAR 002:030, 201 KAR 002:360 and 201 KAR 002:460
- Functionally the amendment allows a pharmacist to supply naloxone to an emergency department to be dispensed per protocol to an individual while also allowing the pharmacist one pharmacy business day to review the dispensing record.
 - This effectively removes legal barriers to hospital emergency departments dispensing take home naloxone to someone that might present to the ED when time with the patient is often short due to patients leaving AMA.
- Full text can be found at pharmacy.ky.gov, under the Statutes and Regulations section, at the bottom of the page under Recently Effective Regulations and Amendments or by scanning this QR code:

<https://pharmacy.ky.gov/statutesandregulations/Documents/201%20KAR%202%20360%20Naloxone%20in%20Emergency%20Departments.pdf>



Kentucky Naloxone Copay Assistance Program

- The Kentucky Opioid Response Effort (KORE) grant has a copay assistance program for naloxone at outpatient / retail pharmacies
- Program can be used to bill the copay of commercial insurance plans or for uninsured / cash patients.
- For OTC Narcan, the program can serve as a coupon if the insurance does not cover the product.
- **Maximum benefit paid is \$45**



The image shows a promotional graphic for the Kentucky Naloxone Copay Program. At the top left is the KORE logo (Kentucky Opioid Response Effort) and at the top right is the Kentucky Pharmacists Association logo. The main title is "Kentucky Naloxone Copay Program". Below this, on an orange background, it says "Pay as little as \$0*" for most naloxone products, including Narcan, Kloxxado, Zimhi, and generics. On a dark blue background, a white box contains the following information: ID: 1396065983, RxBIN: 610524, RxPCN: Loyalty, RxGRP: 50778063, and ISSUER: (80840). A small disclaimer at the bottom right of the blue area states: "*Maximum benefit of \$45 per unit. Some exclusions apply; see reverse for details."

Details can be found at <http://www.kphanet.org/copay> or scan the QR Code:



References

- [ACMT and AACT Position Statement: Preventing Occupational Fentanyl and Fentanyl Analog Exposure to Emergency Responders - PMC \(nih.gov\)](#)
- [Accidental Occupational Exposure to a Large Volume of Liquid Fentanyl on a Compromised Skin Barrier with No Resultant Effect - PubMed \(nih.gov\)](#)
- [Can touch this: training to correct police officer beliefs about overdose from incidental contact with fentanyl | Health & Justice | Full Text \(biomedcentral.com\)](#)
- [Final STANDARD size of Fentanyl Safety Recommendations for First Respond....pdf \(dea.gov\)](#)
- <https://rivive.com/>
- https://www.harmreductiontherapeutics.org/wp-content/uploads/2023/08/HRT-RiVive-Press-Release-July-28-2023-FINAL_DATED.pdf