

Designing a rescue medication for adulterated opioids: OX390 program and BARDA partnership

Animal tranquilizers xylazine and medetomidine are being mixed with illicit opioids, and this appears to be increasing the risk of people dying from overdoses, in addition to profound physical and mental harms. In this interview, Edward Kim, MD, MBA and Chief Medical Officer at Orexo shares his insights into the evolving opioid epidemic and how partnering with Centre for the Biomedical Advanced Research and Development Authority (BARDA), is accelerating research and development of OX390, an innovative rescue treatment.

What are xylazine and medetomidine and how are they affecting the US opioid epidemic?

Xylazine and medetomidine are animal tranquilizers never approved for human use, yet both have entered the illicit drug supply. Xylazine has been found since the 1990s and linked to overdose deaths since the mid-2000s, prompting the White House in 2023 to declare fentanyl-xylazine mixtures an emerging public health threat.¹ Medetomidine, detected in Philadelphia in early 2024, is 50 to 100 times more potent than xylazine and has quickly replaced it in that region.^{2 3}

Acting on the same alpha-2 receptors, these drugs cause severe withdrawal symptoms and complicate treatment because clinicians often do not realize patients have taken adulterated opioids because they're still relatively new to the drug supply and routine surveillance is not universal.⁴

Data on alpha-2 agonists hasn't been tracked nationally for long, but according to available data deaths involving fentanyl mixed with xylazine surged from 99 in 2018 to 6,020 in 2023.⁵ Recent research with mice has shown that the lethality of fentanyl is increased 100 times over when xylazine is added.⁶ If this is the case in humans, we may see a shift where naloxone continues to lower the overall overdose death rate, while deaths from adulterated opioids may continue to grow.

Why are these drugs being combined with opioids?

We don't know for sure. There was a time when illicit opioid suppliers would use inactive fillers to stretch their supplies of the active opioid ingredient and increase profitability. This may still be happening because



*Edward Kim, MD, MBA and
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OX390 program – At a Glance

Platform: AmorphOX®

Goal: Rescue treatment for overdoses from adulterated opioids unresponsive to naloxone.

Unique: No competitors of today. Protected by AmorphOX patents.

Partnership: With BARDA (valued up to USD 51 m) for development through FDA approval. Orexo keeps commercial rights.

Next step: In-vivo proof-of-concept. FDA discussions on IND completed.



xylazine has sedative properties that can mask some of the effects of having a reduced amount of the opioid in a product.

However, it's also possible that drug cartels are using xylazine and medetomidine to enhance the addictive potential of their opioids. The published literature in this area is only just emerging, so we'll need to wait and see, which is the tragedy of it all. Our science is still far behind the problem, and we need to catch up.

What happens in the body when opioids and xylazine are combined?

When opioids are adulterated with xylazine, users can experience extreme sedation, a dangerous drop in their heart rate (bradycardia) and respiratory depression. In severe cases this progresses into respiratory and/or cardiac arrest, and in the absence of an effective rescue medication, can lead to death. If someone doesn't die, they experience a loss of body tone that causes a slumped-over posture, which has led to the term, 'zombie drug'. Disfiguring sores develop on the skin that resemble burns. These can lead to severe infection and even amputation. Following chronic use, people can become dependent on xylazine and experience severe, life-threatening withdrawal when they discontinue. This is because xylazine acts very much like antihypertensive medications, and withdrawal can cause cardiovascular over-stimulation.

Why does naloxone 'sometimes work — but not enough'?

This is what the family members and first responders who treat people streetside tell us.

When patients are in a hospital setting, clinicians have a range of treatments available, including high doses of naloxone that can be administered intravenously. They also have oxygen therapy and respiratory equipment for patients who can't breathe on their own. But streetside, we know that treatment with naloxone alone for overdoses caused by adulterated drugs may not be enough to revive them.

Naloxone doesn't block the brain receptors that xylazine and medetomidine bind to. We're hearing from first responders and others in the harm reduction community that naloxone on its own is much less effective in the neighbourhoods where xylazine is prevalent. Patients don't wake up in the way they used to... their breathing is very laboured and they're difficult to bring back.

Families and caregivers live with the anxiety that the naloxone they have ready to give to their loved one may not be enough to save their life. And for those who are un-sheltered and living on the streets, the dangers are amplified.

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Are there approved treatments for overdoses involving xylazine or other alpha-2 agonists?

No, and that's leaving a vacuum of unmet medical need.

At Orexo, we're developing OX390 to meet this need. It's a rescue medication specifically designed to treat overdoses caused by opioids that are adulterated with xylazine or medetomidine. At the moment, we're in the pre-clinical stage with this product, which uses our own drug delivery platform AmorphOX®. The unique aspect of AmorphOX is that it's a nasal powder, which makes it very quick and easy to administer to someone, even if they're unconscious and not breathing. It absorbs rapidly in the nose and



doesn't run down the throat like liquid sprays. And because it's a powder, OX390 won't freeze during the cold winter months, which is a very real challenge with naloxone that's stored outside in free dispensers.

How is BARDA's collaboration accelerating Orexo's development of rescue therapies?

The BARDA (Centre for the Biomedical Advanced Research and Development Authority) collaboration enhances our ability to make OX390 available to patients sooner. BARDA recognize the unmet need and as they're a federal agency, they're also in a position to make more people aware of the extent of the public health risk adulterated drugs are causing. In addition to the substantial financial commitment, we'll also benefit from the internal subject matter experts at BARDA to help us design an efficient drug development plan. This is more than government funding, it's a true public-private partnership.

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What impact could OX390 have on overdose survival rates and community confidence?

Once we've developed a safe and efficacious product, we'll be able to use our established supply chain to scale production. This supply chain is already in use for our more advanced pipeline products, and is designed to meet the stringent requirements for reliability, quality and stability in a rescue medication.

Our hope is to be able to reduce the number of overdose deaths caused by xylazine or medetomidine by making OX390 available to anyone who needs it so they might live long enough to begin or continue their recovery journey.

Written by Georgina Hoy

¹ <https://bidenwhitehouse.archives.gov/ondcp/briefing-room/2023/04/12/biden-harris-administration-designates-fentanyl-combined-with-xylazine-as-an-emerging-threat-to-the-united-states/>

² <https://hip.phila.gov/document/4421/PDPH-HAN-0441A-05-13-24.pdf/>

³ <https://pubmed.ncbi.nlm.nih.gov/40990306/#:~:text=Abstract,;%20overdose;%20withdrawal;%20xylazine.>

⁴ <https://pubmed.ncbi.nlm.nih.gov/40990306/#:~:text=Abstract,;%20overdose;%20withdrawal;%20xylazine.>

⁵ <https://injuryprevention.bmj.com/content/early/2025/04/01/ip-2024-045596>

⁶ [https://pmc.ncbi.nlm.nih.gov/articles/PMC10557575/#:~:text=Lethality%20was%20not%20as%20rapid,for%20females%20\(Table%201\)](https://pmc.ncbi.nlm.nih.gov/articles/PMC10557575/#:~:text=Lethality%20was%20not%20as%20rapid,for%20females%20(Table%201))

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About Orexo

Orexo is a Swedish pharmaceutical company with 30 years of experience developing improved pharmaceuticals based on proprietary formulation technologies that meet large medical needs. On the US market, Orexo provides innovative treatment solutions for patients suffering from opioid use disorder. Products targeting other therapeutic areas are developed and commercialized worldwide with leading partners. Total net sales in 2024 amounted to SEK 590 million, and the number of employees 110. Orexo is listed on Nasdaq Stockholm's main list and is available as ADRs (ORXOY) on the OTCQX market in the US.

For more information on Orexo, visit www.orexo.com. You can also follow Orexo on X, LinkedIn, and YouTube.