NOVEL PSYCHOACTIVE SUBSTANCES: MEDETOMIDINE

The Legislative Analysis and Public Policy Association (LAPPA) continues to monitor the emergence of novel psychoactive substances (NPS) appearing on the illicit drug market in the United States. The term "novel" does not denote a brand new, never-before-seen substance but rather a substance that is newly available in the drug market. This fact sheet, the seventh in a series highlighting these dangerous drugs, is an examination of medetomidine, a powerful veterinary sedative that has been appearing as an adulterant in fentanyl mixtures in the U.S.

Medetomidine is a synthetic alpha-2 agonist that is used as a sedative in veterinary medicine and sold under the brand name Domitor®. Medetomidine belongs to the same drug class as xylazine, but its potency is 200 times greater, and has a longer duration of action, than xylazine.[1] The U.S. Food and Drug Administration (FDA) has only approved medetomidine for use in veterinary medicine, and information about the use of the substance in humans is limited. However, another form of medetomidine called dexmedetomidine (sold under the brand names Dexdor® and Precedex®) is approved by the FDA as a sedative for human use.

According to the Center for Forensic Science Research and Education, medetomidine first appeared in the illicit drug supply in Maryland in July 2022 alongside fentanyl, xylazine, and other substances.[2] During mid-to-late 2023, scientists sporadically identified medetomidine, most commonly with fentanyl, in toxicology specimens collected from patients presenting to emergency departments after suspected opioid overdoses in California, Colorado, Florida, Maryland, Missouri, North Carolina, Ohio, and Pennsylvania.[3] In April 2024, drug products adulterated with medetomidine resulted in a large scale outbreak of non-fatal overdoses and adverse events in Philadelphia, Pennsylvania, with nearly 100 individuals effected over the course of three days.[4] A month later, scientists identified drug products adulterated with medetomidine for the first time in Pittsburgh, Pennsylvania and Chicago, Illinois after both cities experienced a spike in non-fatal overdoses.[5] Researchers are not sure why medetomidine has been appearing in the illicit drug market recently, but they hypothesize that it might be in response to the tightened controls that states and the federal government have been implementing with respect to xylazine. It is also unclear whether the medetomidine in the illicit drug market is being illegally diverted from veterinary supplies or if drug traffickers are producing their own medetomidine compounds from precursor chemicals. Unlike test strips for fentanyl and xylazine, direct to consumer devices to test for medetomidine do not currently exist.

The effects of medetomidine on humans are not well understood but include prolonged sedation, slow heart rate (*i.e.*, bradycardia), slowed breathing, and low blood pressure. Similar to xylazine, the combination of medetomidine with other substances, like fentanyl, can enhance or prolong the effects of the substance and place the individual at a higher risk of overdose than from the substance alone. It is unknown if medetomidine use in humans will produce wounds like those associated with xylazine. Medetomidine is not an opioid and thus, does not respond to opioid antagonists, such as naloxone, but drug experts recommend administering an opioid antagonist to individuals suspected to be experiencing a medetomidine overdose nonetheless due to the substance commonly being mixed with fentanyl. There are two medications, atipamezole (sold under the brand name Antisedan®) and yohimbine, that can be used to reverse the effects of medetomidine in animals, but these substances are not approved for use in humans by the FDA, so drug researchers

[1] Anna R. Connell, et al., "Comparisons of α2-Adrenergic Agents, Medetomidine and Xylazine, with Pentobarbital for Anesthesia: Important Pitfalls in Diabetic and Nondiabetic Rats," *Journal of Ocular Pharmacology and Therapeutics* 38, no. 2 (March 2022): 157, https://doi.org/10.1089/jop.2021.0084.
[2] Alex Krotulski, et al., "Medetomidine Rapidly Proliferating Across USA — Implicated In Recreational Opioid Drug Supply & Causing Overdose Outbreaks," *Center for Forensic Science Research and Education*, May 20, 2024, https://www.cfsre.org/nps-discovery/public-alerts/medetomidine-rapidly-proliferating-across-usa-implicated-in-recreational-opioid-drug-supply-causing-overdose-outbreaks.
[3] *Id.*
[4] *Id. See also* "Adulterant Alert: Medetomidine, Update and Analysis," PA Groundhogs, accessed June 21, 2024, https://img1.wsimg.com/blobby/go/cdb7878c-6841-411b-ade7-1013bc27480d/26858440.Update__16_May_06_10_PM-3.pdf.
[5] Krotulski, *supra* note 2.

do not recommend using them to reverse medetomidine overdose in humans. Individuals experiencing a medetomidine overdose should be managed with evidence-based critical care, such as airway management and cardiovascular support. Medetomidine withdrawal is not well described in the medical literature, but it is likely similar to dexmedetomidine withdrawal, which includes high blood pressure, rapid heart rate, and agitation.

Medetomidine is not federally controlled under the Controlled Substances Act, but the substance is federally restricted to the use by or on the order of a licensed veterinarian (21 C.F.R. § 522.1335 (2024)). Currently, there are not any federal efforts to schedule medetomidine. Additionally, no state nor the District of Columbia schedule medetomidine, and there are not any proposed bills to schedule the substance in any state or the District of Columbia. Like with xylazine, any future attempts to schedule medetomidine on either the state or federal level will have to consider the use and legitimate supply of medetomidine in veterinary medicine.

CONCLUSION

There remain many unknowns about the use of medetomidine in humans, but the substance's effect of prolonged sedation presents a public health concern. While medetomidine has only been found in a handful of jurisdictions (mostly in the Northeast and the Midwest) thus far, it is possible that the substance will continue to spread across the country as xylazine becomes more expensive and difficult to obtain as a result of increased federal and state regulation and penalties. Should states and the federal government wish to schedule medetomidine in the future, it will be important to ensure legitimate access to the substance for veterinary medicine practices.

RESOURCES

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Midthun, Kari, et al. "Toxic Adulterant Alert: Medetomidine/Dexmedetomidine." *Center for Forensic Science Research and Education*, December 2023. https://www.cfsre.org/nps-discovery/public-alerts/toxic-adulterant-alert-medetomidine-dexmedetomidine.

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The Legislative Analysis and Public Policy Association (LAPPA) is a 501(c)(3) nonprofit organization whose mission is to conduct legal and legislative research and analysis and draft legislation on effective law and policy in the areas of public safety and health, substance use disorders, and the criminal justice system.

LAPPA produces up-to-the-minute comparative analyses, publications, educational brochures, and other tools ranging from podcasts to model laws and policies that can be used by national, state, and local criminal justice and substance use disorder practitioners who want the latest comprehensive information on law and policy. Examples of topics on which LAPPA has assisted stakeholders include naloxone laws, treatment in emergency settings, alternatives to incarceration for those with substance use disorders, medication for addiction treatment in correctional settings, and syringe services programs.

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