

NOVEL PSYCHOACTIVE SUBSTANCES: TIANEPTINE

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The Legislative Analysis and Public Policy Association (LAPPA) is monitoring the emergence of novel psychoactive substances (NPS) appearing on the illicit drug market in the United States. The term “novel” does not denote a new, never-before-seen substance but rather a substance that is newly available in the drug market. This fact sheet, the third in a series highlighting these potentially dangerous drugs, examines tianeptine, an unapproved drug commonly sold in gas stations and on the internet as a dietary supplement and causes opioid-like withdrawals.

Discovered and patented in the 1960s, tianeptine is an antidepressant drug structurally similar to tricyclic antidepressants that is sold as a prescription medication under the brand names Coaxil and Stablon in some European, Asian, and Latin American countries.¹ In the United States, however, tianeptine is not a drug approved by the Food and Drug Administration (FDA). Despite not being an FDA approved drug, tianeptine is available for purchase in the U.S. as a dietary supplement under brand names such as “Zaza Red,” “TD Red,” and “Tianna.” Dietary supplements containing tianeptine can be purchased in gas stations, head shops, and on the internet. Ads for supplements containing tianeptine claim that the product reduces pain and provides stress relief.

Animal and human studies show that tianeptine is a mu-opioid receptor agonist.² For this reason, experts believe that individuals who ingest tianeptine may develop a dependence and addiction to the substance. This risk increases for individuals with a history of opioid misuse and addiction, and FDA reports suggest that adverse events may occur when an individual takes tianeptine at high doses. Several case studies show that tianeptine toxicity mimics opioid toxicity and that individuals experience tianeptine withdrawal symptoms similar to those of opioid withdrawal. There are also reports of infants experiencing withdrawal from tianeptine, with symptoms that mimic those of infants withdrawing from opioid dependence, after tianeptine use during pregnancy. The parallels between opioids and tianeptine, coupled with tianeptine’s availability at gas stations, led to the media nicknaming the substance “gas station heroin.” Similar to heroin, naloxone reverses the effects of an overdose from tianeptine.

Tianeptine use in the U.S. has been on the rise in recent years. A 2018 study published in the *Morbidity and Mortality Weekly Report* issued by the U.S. Centers for Disease Control and Prevention examined calls to U.S. poison control centers between 2000 and 2017 for tianeptine exposure.³ The study found that in the 14 years between 2000 and 2013, the National Poison Data System (NPDS) received a total of 11 tianeptine exposure calls.⁴ Starting in 2014, however, the number of tianeptine exposure calls increased exponentially, with five calls in 2014, 38 in 2015, 83 in 2016, and 81 in 2017.⁵ The researchers hypothesized that the increase in calls starting in 2014 might be due to individuals learning of the 2014 study finding tianeptine to be an effective mu-opioid receptor agonist and thus reasoning that it could be a viable opioid alternative.

¹ Tricyclic antidepressants are a class of medications used in the management and treatment of major depressive disorder. They are second-line treatments, usually considered after trying selective serotonin reuptake inhibitors (SSRIs). Jordan Moraczewski and Kapil K. Aedma, “Tricyclic Antidepressants,” National Institutes of Health, National Library of Medicine (Nov. 21, 2022), <https://www.ncbi.nlm.nih.gov/books/NBK557791/>.

² Mu-opioid receptors are a type of receptor in the brain that is responsible for pain control, drug reward, and addictive behaviors. Mu-opioid receptor agonists, such as morphine and heroin, effectively bind to mu-opioid receptors and produce a physiological response in the body. Gavril W. Pasternak and Ying-Xian Pan, “Mu-opioids and Their Receptors: Evolution of a Concept,” *Pharmacological Reviews* 64, no. 4 (October 2013): 1257-1317, <https://doi.org/10.1124/pr.112.007138>.

³ Tharwat El Zahran, et al., “Characteristics of Tianeptine Exposures Reported to the National Poison Data System- United States, 2000-2017,” *Morbidity and Mortality Weekly Report* 67, no. 30 (August 2018): 815-818, <https://www.cdc.gov/mmwr/volumes/67/wr/pdfs/mm6730a2-H.pdf>.

⁴ *Id.* at 815.

⁵ *Id.* at 816.

Of the 218 calls that the NPDS received related to tianeptine exposure between 2000 and 2017, tianeptine-only exposures accounted for 114 calls.⁶ In the remaining polysubstance calls, the most often reported substances in addition to tianeptine included phenibut (a central nervous system depressant), ethanol, benzodiazepines, and opioids.⁷ Among the 114 tianeptine-only exposures, the most commonly reported clinical effects were neurologic, cardiovascular, and gastrointestinal.⁸ The NPDS data also showed 29 tianeptine associated withdrawal calls between 2000 and 2017, with tianeptine being the only substance reported in 21 of those calls.⁹ Among those 21 calls, the most frequently reported signs and symptoms included agitation, nausea, increased heart rate, and high blood pressure.¹⁰

Beyond the nonfatal tianeptine poisonings reported in the U.S. and internationally, prior to 2018, scientific literature contained reports of only two fatal overdoses, both occurring outside of the U.S.¹¹ In 2018, an article published in the *Journal of Analytical Toxicology* reported two fatalities involving tianeptine in Texas. These two fatalities may be the first known tianeptine fatalities in the U.S.¹² In November 2018, the FDA published an alert for consumers about tianeptine in dietary supplements.¹³ The alert stated that “tianeptine is a substance that does not meet the statutory definition of a dietary ingredient and is an unsafe food additive” and as a result, dietary supplements containing tianeptine are “adulterated” under the Federal Food, Drug, and Cosmetic Act.¹⁴ The FDA advised consumers to avoid all products containing tianeptine, especially any claiming to treat opioid use disorder.¹⁵ The FDA released another alert about tianeptine in February 2022, stating that companies continue to illegally market and sell products containing tianeptine to consumers and continue to make “dangerous and unproven claims that tianeptine can improve brain function and treat anxiety, depression, pain, opioid use disorder, and other conditions.”¹⁶ According to the FDA’s February 2022 alert, poison control cases involving tianeptine totaled 151 in 2020.¹⁷ Since 2020, there has been little published data about adverse tianeptine exposures.

Despite the FDA-issued alerts, tianeptine is not a controlled substance under the federal Controlled Substances Act. While there has not been any federal action to control tianeptine, some states control the substance through legislation. As of March 2023, four states (Alabama,¹⁸ Georgia,¹⁹ Minnesota,²⁰ and Ohio²¹) list tianeptine as a Schedule I controlled substance, while four others (Arkansas,²² Michigan,²³ Oklahoma,²⁴ and Tennessee²⁵) list tianeptine as a Schedule II controlled substance. The split in scheduling among these eight states suggests that there is no universal conclusion about the medical usefulness (or lack thereof) of tianeptine.²⁶

⁶ *Id.*

⁷ *Id.*

⁸ *Id.*

⁹ *Id.*

¹⁰ *Id.*

¹¹ Erica L. Bakota, et al., “Case Reports of Fatalities Involving Tianeptine in the United States,” *Journal of Analytical Toxicology* 42, no. 7 (September 2018): 503-509, <https://doi.org/10.1093/jat/bky023>.

¹² *Id.*

¹³ “Tianeptine in Dietary Supplements,” U.S. Food and Drug Administration, last modified November 20, 2018, <https://www.fda.gov/food/dietary-supplement-products-ingredients/tianeptine-dietary-supplements>.

¹⁴ *Id.*

¹⁵ *Id.*

¹⁶ “Tianeptine Products Linked to Serious Harm, Overdoses, Death,” U.S. Food and Drug Administration, last modified February 10, 2022, <https://www.fda.gov/consumers/consumer-updates/tianeptine-products-linked-serious-harm-overdoses-death>.

¹⁷ *Id.*

¹⁸ ALA. CODE § 20-2-23 (2022). Tianeptine scheduled effective May 1, 2021.

¹⁹ GA. CODE ANN. § 16-13-25 (West 2022). Tianeptine scheduled effective May 13, 2022.

²⁰ MINN. STAT. ANN. § 152.02 (West 2023). Tianeptine scheduled effective August 1, 2018.

²¹ OHIO ADMIN. CODE 4729:9-1-01.3 (West 2022). Tianeptine scheduled effective December 22, 2022.

²² 007.07.2 ARK. CODE R. § 2 (West 2022). Tianeptine scheduled effective May 2, 2022.

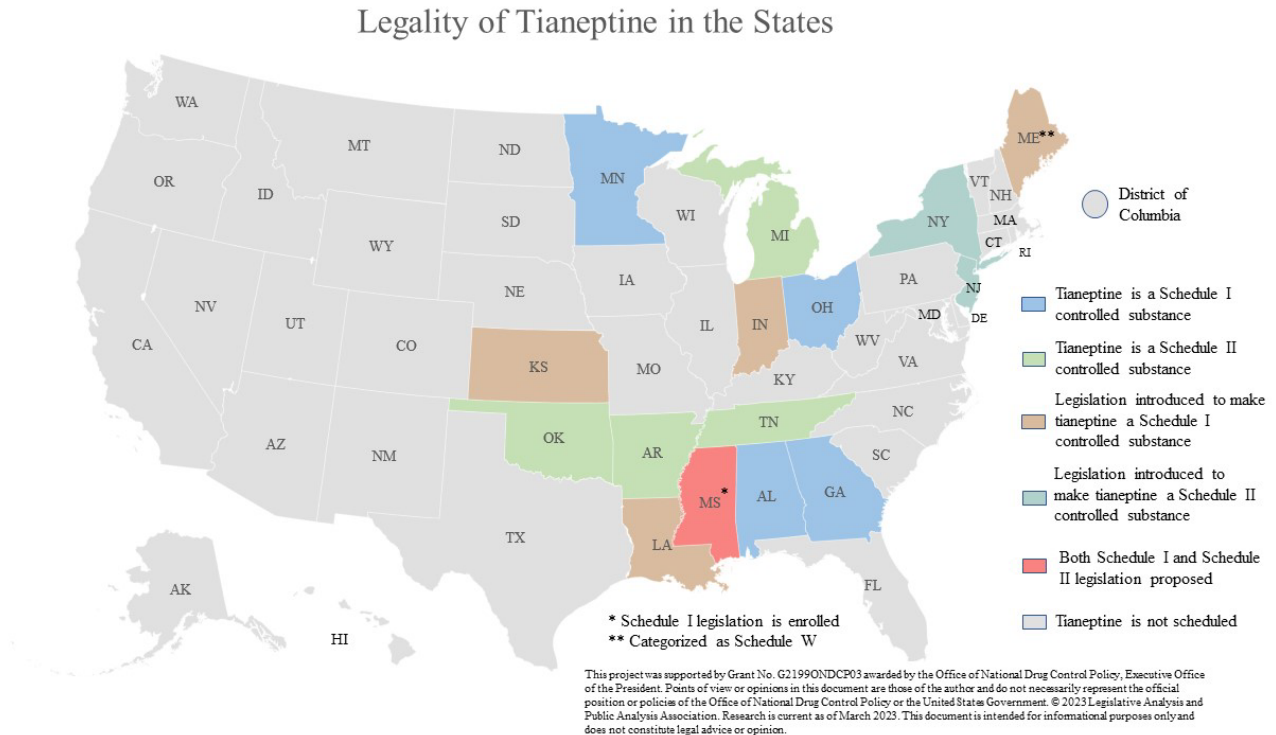
²³ MICH. COMP. LAWS ANN. § 333.7214 (West 2022). Tianeptine scheduled effective July 4, 2018.

²⁴ OKLA. STAT. ANN. tit. 63 § 2-206 (West 2022). Tianeptine scheduled effective November 1, 2019.

²⁵ TENN. CODE ANN. § 39-17-408 (West 2022). Tianeptine scheduled effective July 1, 2022.

²⁶ Schedule I drugs are drugs with high abuse risk that have no safe, accepted medical uses. In contrast, Schedule II drugs are drugs with a high abuse risk, but with safe and accepted medical uses.

In 2022 and in the first few months of 2023, seven states introduced legislation to control tianeptine. Indiana,²⁷ Kansas,²⁸ and Louisiana,²⁹ have proposed legislation to make tianeptine a Schedule I controlled substance, while New Jersey³⁰ and New York³¹ have proposed legislation to make tianeptine a Schedule II controlled substance. Maine³² has introduced legislation to make tianeptine a Schedule W drug.³³ Earlier this year, Mississippi legislators introduced multiple tianeptine related bills,³⁴ only one of which remains alive and proposes to add tianeptine to Schedule I.³⁵ The bill has passed both chambers of the legislature and is awaiting the governor’s signature. The map below details the legality of tianeptine in the states.



²⁷ S.B. 379, 2023 Gen. Assemb., Reg. Sess. (Ind. 2023) (Senate passed bill on February 9, 2023).

²⁸ S.B. 9, 2023-2024 Leg., Reg. Sess. (Kan. 2023).

²⁹ H.B. 382, 2022 Leg., Reg. Sess. (La. 2022) (died upon legislature’s adjournment).

³⁰ S. 3668, 2023-2023 Leg., Reg. Sess. (N.J. 2023).

³¹ S.B. 1720, 2023-2024 Leg., Reg. Sess. (N.Y. 2023) and A. 344, 2023-2024 Leg., Reg. Sess. (N.Y. 2023).

³² H.P. 517, 131st, Leg., Reg. Sess. (Me. 2023).

³³ Unlike the federal government and most states, which categorize controlled substances into Schedules I-V, Maine categorizes its drugs into Schedules W, X, Y, and Z. Maine’s Schedule W category is akin a Schedule I category.

³⁴ As compared to other states, Mississippi legislators introduced a number of unique tianeptine related legislation. This included House Bill 838, which proposed to create the “Mississippi Tianeptine Consumer Protection Act” (H.B. 838, 2023 Leg., Reg. Sess. (Miss. 2023) (died in committee)) which would have: (1) required tianeptine processors to register and pay an annual registration fee in order to sell tianeptine products in the state; (2) prohibited the sale of tianeptine products without adequate labeling necessary for the safe and effective use by consumers, including a recommended serving size; (3) prohibited the sale of tianeptine to individuals under the age of 21; and (4) established civil penalties against processors or retailers who violate the Act. Additionally, Mississippi House Bill 1265 (H.B. 1265, 2023 Leg., Reg. Sess. (Miss. 2023) (died in committee)) and Senate Bill 2819 (S.B. 2819, 2023 Leg. Reg. Sess. (Miss. 2023) (died in committee)) proposed to establish a screening and approval program within the state department of health for the over-the-counter availability and retail sale of products that “contain any substance with the potential to be recreationally used or abused.” The purpose of the proposed screening program was to reduce the retail sale and availability of products that contain certain over-the-counter substances, including, but not limited to, bath salts, kratom, and tianeptine. All three bills died in committee earlier this year.

³⁵ H.B. 4, 2023 Leg. Reg. Sess. (Miss. 2023) (enrolled).

While tianeptine is not as dangerous as other NPS, it remains a concern to states and to the FDA due to its ability to produce opioid-like symptoms in individuals taking the substance in high doses. LAPPa will continue to monitor its spread and any new regulatory responses at the state or federal level.

RESOURCES

Manisha Krishnan, “‘Gas Station Heroin’ is Causing Intense Withdrawals. It’s Legal in Most States,” *Vice*, December 12, 2022, <https://www.vice.com/en/article/88q3va/tianeptine-gas-station-heroin-legal-in-most-states>.

“Tianeptine,” U.S. Drug Enforcement Administration, last modified January 2023, https://www.deadiversion.usdoj.gov/drug_chem_info/tianeptine.pdf.

ABOUT LEGISLATIVE ANALYSIS AND PUBLIC POLICY ASSOCIATION

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 timely model laws and policies that can be used by national, state, and local public health, public safety, and substance use disorder practitioners who want the latest comprehensive information on law and policy as well as up-to-the-minute comparative analyses, publications, educational brochures, and other tools ranging from podcasts to fact sheets. Examples of topics on which LAPPa has assisted stakeholders include law enforcement/community engagement, naloxone laws, alternatives to incarceration for those with substance use disorders, medication for addiction treatment in correctional settings, and the involuntary commitment and guardianship of individuals with alcohol or substance use disorders.

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