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DEPARTMENT OF JUSTICE

Drug Enforcement Administration

21 CFR Part 1308

[Docket No. DEA1596]

Schedules of Controlled Substances: Placement of Tianeptine in Schedule I

AGENCY: Drug Enforcement Administration, Department of Justice.

ACTION: Notice of proposed rulemaking.

SUMMARY: The Drug Enforcement Administration proposes placing the substance tianeptine (7-[(3-chloro-6,11-dihydro-6-methyl-5,5-dioxidodibenzo[*c,f*][1,2]thiazepin-11-yl)amino]heptanoic acid), including its isomers, esters, ethers, salts, and salts of isomers, esters, and ethers whenever the existence of such isomers, esters, ethers, salts, and salts of isomers, esters, and ethers is possible, in schedule I of the Controlled Substances Act. If finalized, this action would impose the regulatory controls and administrative, civil, and criminal sanctions applicable to schedule I controlled substances on persons who handle (manufacture, distribute, reverse distribute, import, export, engage in research, conduct instructional activities or chemical analysis with, or possess) or propose to handle tianeptine.

DATES: Comments must be submitted electronically or postmarked on or before **[INSERT DATE 30 DAYS AFTER DATE OF PUBLICATION IN THE FEDERAL REGISTER]**. The electronic Federal Docket Management System will not accept comments after 11:59 p.m. Eastern Time on the last day of the comment period.

Interested persons may file a request for a hearing or waiver of hearing pursuant to 21 CFR 1308.44 and in accordance with 21 CFR 1316.47 and/or 1316.49, as applicable. Requests for a hearing and waivers of an opportunity for a hearing or to participate in a hearing, together with a written statement of position on the matters of fact and law asserted in the hearing, must be received or postmarked on or before **[INSERT DATE 30 DAYS AFTER DATE OF PUBLICATION IN THE FEDERAL REGISTER]**.

ADDRESSES: Interested persons may file written comments on this proposal in accordance with 21 CFR 1308.43(g). To ensure proper handling of comments, please reference "Docket No. DEA1596" on all electronic and written correspondence, including any attachments.

- *Electronic comments:* The Drug Enforcement Administration (DEA) encourages commenters to submit comments electronically through the Federal eRulemaking Portal, which provides the ability to type short comments directly into the comment field on the webpage or attach a file for lengthier comments. Please go to *www.regulations.gov* and follow the online instructions at that site for submitting comments. Upon completion of your submission, you will receive a Comment Tracking Number. Submitted comments are not instantaneously available for public view on *www.regulations.gov*. If you have received a Comment Tracking Number, your comment has been successfully submitted and there is no need to resubmit the same comment. Commenters should be aware that the electronic Federal Docket Management System will not accept comments after 11:59 p.m. Eastern Time on the last day of the comment period.

- *Paper comments:* Paper comments that duplicate the electronic submissions are not necessary and are discouraged. Should you wish to mail a paper comment in lieu of an electronic comment, it should be sent via regular or express mail to: Drug Enforcement Administration, Attn: DEA Federal Register Representative/DPW, 8701 Morrissette Drive, Springfield, Virginia 22152.

- *Hearing requests:* All requests for a hearing and waivers of participation, together with a written statement of position on the matters of fact and law asserted in the hearing, must be filed with the DEA Administrator, who will make the determination of whether a hearing will be needed to address such matters of fact and law in the rulemaking. Such requests must be sent to: Drug Enforcement Administration, Attn: Administrator, 8701 Morrissette Drive, Springfield, Virginia 22152. For informational purposes, a courtesy copy of requests for hearing and waivers of participation should also be sent to: (1) Drug Enforcement Administration, Attn: Hearing Clerk/OALJ, 8701 Morrissette Drive, Springfield, Virginia 22152; and (2) Drug Enforcement Administration, Attn: DEA Federal Register Representative/DPW, 8701 Morrissette Drive, Springfield, Virginia 22152.

FOR FURTHER INFORMATION CONTACT: Dr. Terrence L. Boos, Drug and Chemical Evaluation Section, Diversion Control Division, Drug Enforcement Administration; Telephone: (571) 362-3249.

As required by 5 U.S.C. 553(b)(4), a summary of this proposed rule may be found in the docket for this rulemaking at *www.regulations.gov.*

SUPPLEMENTARY INFORMATION: The Drug Enforcement Administration (DEA) proposes placing the substance tianeptine (7-[(3-chloro-6,11-dihydro-6-methyl-

5,5-dioxidodibenzo[*c,f*][1,2]thiazepin-11-yl)amino]heptanoic acid) in schedule I of the Controlled Substances Act (CSA), including its isomers, esters, ethers, salts, and salts of isomers, esters, and ethers whenever the existence of such isomers, esters, ethers, salts, and salts of isomers, esters, and ethers is possible within the specific chemical designation.

Posting of Public Comments

All comments received in response to this docket are considered part of the public record. DEA will make comments available for public inspection online at *http://www.regulations.gov*, unless reasonable cause is given. Such information includes personal or business identifiers (such as name, address, state of federal identifiers, etc.) voluntarily submitted by the commenter.

Commenters submitting comments which include personal identifying information (PII), confidential, or proprietary business information that the commenter does not want to be made publicly available should submit two copies of the comment. One copy must be marked "CONTAINS CONFIDENTIAL INFORMATION" and should clearly identify all PII or business information the commenter does not want to be made publicly available, including any supplemental materials. DEA will review this copy, including the claimed PII and confidential business information, in its consideration of comments. The second copy should be marked "TO BE PUBLICLY POSTED" and must have all claimed confidential PII and business information already redacted. DEA will post only the redacted comment on *http://www.regulations.gov* for public inspection. DEA generally will not redact additional information contained in the

comment marked "TO BE PUBLICLY POSTED." The Freedom of Information Act applies to all comments received.

For easy reference, an electronic copy of this document and supplemental information to this proposed scheduling action are available at *http://www.regulations.gov*.

Request for Hearing or Appearance; Waiver

Pursuant to 21 U.S.C. 811(a), this action is a formal rulemaking "on the record after opportunity for a hearing." Such proceedings are conducted pursuant to the provisions of the Administrative Procedure Act (APA).[1] Interested persons, as defined in 21 CFR 1300.01(b), may file requests for a hearing in conformity with the requirements of 21 CFR 1308.44(a) and 1316.47(a), and such requests must:

(1) state with particularity the interest of the person in the proceeding;

(2) state with particularity the objections or issues concerning which the person desires to be heard; and

(3) state briefly the position of the person regarding the objections or issues.

Any interested person may file a waiver of an opportunity for a hearing or to participate in a hearing in conformity with the requirements of 21 CFR 1308.44(c), together with a written statement of position on the matters of fact and law involved in any hearing.[2]

All requests for a hearing and waivers of participation, together with a written statement of position on the matters of fact and law involved in such hearing, must be sent to DEA using the address information provided above. The decision whether a

[1] 5 U.S.C. 551–559; 21 CFR 1308.41–1308.45; 21 CFR part 1316, subpart D.
[2] 21 CFR 1316.49.

hearing will be needed to address such matters of fact and law in the rulemaking will be made by the Administrator. If a hearing is needed, DEA will publish a notice of hearing on the proposed rulemaking in the *Federal Register*.[3] Further, once the Administrator determines a hearing is needed to address such matters of fact and law in rulemaking, he will then designate an Administrative Law Judge (ALJ) to preside over the hearing. The ALJ's functions shall commence upon designation, as provided in 21 CFR 1316.52.

In accordance with 21 U.S.C. 811 and 812, the purpose of a hearing would be to determine whether tianeptine meets the statutory criteria for placement in schedule I, as proposed in this rulemaking.

Legal Authority

The CSA provides that proceedings for the issuance, amendment, or repeal of the scheduling of any drug or other substance may be initiated by the Attorney General (delegated to the Administrator of DEA pursuant to 28 CFR 0.100) on her own motion, at the request of the Secretary of Health and Human Services (HHS), or on the petition of an interested party.[4] This proposed action is initiated on the Administrator's own motion and supported by, *inter alia*, a recommendation from the then-Assistant Secretary for Health (Assistant Secretary) of HHS and an evaluation of all other relevant data by DEA. If finalized, this action would impose the regulatory controls and administrative, civil, and criminal sanctions applicable to schedule I controlled substances on any person who handles or proposes to handle tianeptine.

Pursuant to 21 U.S.C. 811(a)(1), the Attorney General (as delegated to the Administrator of DEA) may, by rule, and upon the recommendation of the Secretary, add

[3] 21 CFR 1308.44(b), 1316.53.
[4] 21 U.S.C. 811(a).

to such a schedule or transfer between such schedules any drug or other substance, if she finds that such drug or other substance has a potential for abuse, and makes with respect to such drug or other substance the findings prescribed by 21 U.S.C. 812(b) for the schedule in which such drug or other substance is to be placed.

Background

Tianeptine is structurally and pharmacologically referred to as a tricyclic antidepressant. However, recent case reports have described the use of tianeptine for its euphoric properties similar to other opioids, such as heroin, morphine, and fentanyl. Severe adverse health effects, including respiratory depression, severe sedation, and death, have occurred from the misuse of tianeptine. The use of tianeptine by both current opioid abusers and opioid-naïve individuals poses a hazard to public safety. There are no tianeptine products approved for medical use in the United States.

Proposed Determination to Schedule Tianeptine

Pursuant to 21 U.S.C. 811(b), DEA gathered the necessary data on tianeptine and, on September 7, 2023, submitted it to the then-Assistant Secretary for Health of HHS with a request for a scientific and medical evaluation of available information and a scheduling recommendation for tianeptine.

On July 18, 2025, HHS provided DEA a scientific and medical evaluation entitled, "Basis for the Recommendation to Place Tianeptine and its salts in Schedule I of the Controlled Substances Act," and a scheduling recommendation. Pursuant to 21 U.S.C. 811(b), following consideration of the eight factors and findings related to the substance's abuse potential, legitimate medical use, and safety or dependence liability, HHS recommended that tianeptine be controlled in schedule I of the CSA under 21

U.S.C. 812(b). HHS noted that tianeptine is a tricyclic antidepressant that has been shown to have pharmacological effects similar to opioids currently scheduled under the CSA, such as morphine (schedule II) and fentanyl (schedule II). Although tianeptine is approved for medical use in European, Asian, and Latin American countries as a prescribed drug typically used for depression, there are no tianeptine products approved for medical use in the United States. HHS detailed that health care practitioners and medical examiners have reported cases of severe adverse events and even death involving the ingestion of tianeptine.

In response, DEA reviewed the scientific and medical evaluation and scheduling recommendation provided by HHS, and all other relevant data, and conducted its own eight-factor analysis in accordance with 21 U.S.C. 811(c). Included below is a brief summary of each factor as analyzed by HHS and DEA in their respective eight-factor analyses, and as considered by DEA in this proposed scheduling determination. Please note that both the DEA and HHS analyses, including the evaluation of the eight factors determinative of control along with their supporting data and citations, are available in their entirety under the tab "Supporting Documents" of the public docket of this proposed rule at *https://www.regulations.gov*, under docket number DEA1596.

1. *Its actual or relative potential for abuse*

In addition to considering the information HHS provided in its scientific and medical evaluation document for tianeptine, DEA also considered all other relevant data regarding actual or relative potential for abuse of tianeptine. The term "abuse" is not defined in the CSA; however, the legislative history of the CSA suggests considering the

following four prongs in determining whether a particular drug or substances has a potential for abuse:[5]

> *a. There is evidence that individuals are taking the drug or drugs containing such a substance in amounts sufficient to create a hazard to their health or to the safety of other individuals or of the community; or*
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> *b. There is significant diversion of the drug or substance from legitimate drug channels; or*
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> *c. Individuals are taking the drug or drugs containing such a substance on their own initiative rather than on the basis of medical advice from a practitioner licensed by law to administer such drugs in the course of his professional practice; or*
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> *d. The drug or drugs containing such a substance are new drugs so related in their action to a drug or drugs already listed as having a potential for abuse to make it likely that the drug will have the same potentiality for abuse as such drugs, thus making it reasonable to assume that there may be significant diversions from legitimate channels, significant use contrary to or without medical advice, or that it has a substantial capability of creating hazards to the health of the user or to the safety of the community.*

Both the DEA and HHS eight-factor analyses found that tianeptine produces pharmacological effects that are similar to those produced by schedule II opioids, including morphine and fentanyl. The abuse of tianeptine has been shown to result in respiratory depression, seizures, opioid withdrawal symptoms, and death. While recommended therapeutic dosing of tianeptine in countries where it is legal is 12.5 milligrams (mg) three times per day, recent alerts from the U.S. Food and Drug Administration (FDA) have reported that labels on products sold within the United States indicate that some products contain large amounts of tianeptine ranging from hundreds to over 1,000 mg per dosage unit. In a recent alert, FDA cited multiple case reports in the medical literature that describe United States consumers ingesting daily doses on the

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[5] Comprehensive Drug Abuse Prevention and Control Act of 1970, H.R. Rep. No. 91-1444, 91st Cong., Sess. 1 (1970); reprinted in 1970 U.S.C.C.A.N. 4566, 4603.

order of 1.3 to 250 times (50 mg to 10,000 mg) the daily tianeptine dose typically recommended in labeled foreign drug products.[6]

Since tianeptine is not an FDA-approved product, there are no legitimate drug channels for this substance as a marketed drug in the United States. With no legitimate sources for tianeptine within the United States outside of legitimate chemical manufacturers for research purposes, and HHS' indication that tianeptine is not an FDA-approved product for treatment within the United States, tianeptine use is resultant of users purchasing this product from illegitimate sources.

There are numerous case reports detailing serious adverse reactions, including death, following the use of tianeptine. Individuals are using tianeptine in a manner similar to other opioids, such as heroin, morphine, or fentanyl, to achieve a euphoric state. Scientific reports have detailed escalating use of tianeptine in supratherapeutic doses that have shown to be deleterious to the user's health. Serious withdrawal symptoms following tianeptine abuse have been reported. Tianeptine abuse is associated with psychological and physical dependence. HHS also noted that naloxone administration has been shown in some cases to reverse tianeptine overdose, which supports that tianeptine effects are mediated, at least in part, through its mu opioid agonist activity.

Amidst the current opioid epidemic, users are constantly searching out new substances, with often similar or increased danger to the user, to feed their addiction. In addition, some users have attempted to self-medicate using online drugs such as tianeptine, marketed as "addiction remedies." While some users seek out substances to

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[6] FDA, New "Gas Station Heroin" Tianeptine Product Trend (May 8, 2025), *available at* https://www.fda.gov/consumers/health-fraud-scams/new-gas-station-heroin-tianeptine-product-trend.

curb withdrawal symptoms from other opioids, select individuals try new substances to gain a novel high from the substance or to evade drug tests that more commonly known substances trigger.

In agreement with HHS, DEA believes that, taken together, subsections (a) through (d) of Factor 1 indicate that tianeptine has a relative potential for abuse that is similar to other opioid agonists controlled under the CSA, such as morphine (schedule II) and fentanyl (schedule II).

2. *Scientific evidence of the drug's pharmacological effects, if known*

As explained in the eight-factor analyses by HHS and DEA, the available pharmacology data indicate that tianeptine exerts its mechanism of action via activation of select opioid receptors. Various studies using animal models demonstrated that tianeptine administration, similar to morphine, results in mu-opioid agonist effects. While animal studies initially reported that tianeptine administered systemically increases respiratory output and prevents morphine-induced respiratory depression in rats without affecting its analgesic effects, clinical effects in humans produced analgesia and respiratory depression following the use of tianeptine. One possibility to explain these disparate findings in rat and human respiratory effects is that the effects of tianeptine are biphasic, in that at low doses, tianeptine can both increase respiration and/or prevent morphine-induced respiratory depression; however high doses, representative of a person abusing tianeptine, can result in respiratory depression similar to other opioids, such as morphine or fentanyl. In its review, HHS described the results of the drug discrimination assay following the administration of tianeptine. In these studies, rats were trained to discriminate the effects of the mu-opioid agonist morphine from saline. When the

morphine-trained rats were challenged with tianeptine, full generalization to morphine occurred (i.e., the rats could not differentiate between morphine and tianeptine). Thus, the drug discrimination data demonstrates that tianeptine has pharmacological properties that are similar to morphine, though with less potency. HHS noted that while clinical studies involving tianeptine administration in humans were reviewed, these studies utilized doses that are typically prescribed for use in other countries (i.e., 37.5 mg per day) and are not reflective of doses seen in abuse-related case reports (i.e., hundreds to thousands of milligrams per day). Therefore, due to the limitations of these clinical studies and the higher doses of tianeptine required to produce opioid-like activity, human abuse potential could not be evaluated from these clinical studies.

3. *The state of current scientific knowledge regarding the drug or other substance*

HHS noted that tianeptine is rapidly absorbed in the gastrointestinal tract and has a high bioavailability of approximately 90 to 99 percent. Tianeptine is primarily metabolized in the liver, leading to two major metabolites—MC3 and MC5—with MC5 possessing agonist activity at the mu-opioid receptor. Tianeptine has a half-life of approximately 2.5 hours and is excreted mainly via the kidney. The MC5 metabolite has a longer half-life that can vary between 7.2 and 12.3 hours.

Tianeptine is not an FDA-approved drug in the United States, although it is approved in other countries. Because tianeptine is not FDA-approved, FDA considered both the DEA five-part test and the HHS two-part test to determine whether it has a

currently accepted medical use in treatment in the United States.[7] Ultimately, FDA concluded that tianeptine did not satisfy the DEA five-part test for a currently accepted medical use for treatment in the United States.

FDA further noted that there were no implemented state-authorized programs for the medical use of tianeptine in any state or locality in the United States. Therefore, tianeptine does not satisfy the HHS two-part test for determining whether it has a currently accepted medical use in treatment in the United States.

In conclusion, tianeptine is not FDA-approved, does not meet each of the elements in the DEA five-part test, and does not satisfy the HHS two-part test. Therefore, FDA concluded that tianeptine does not have a currently accepted medical use in treatment in the United States. Similarly, DEA concludes tianeptine has no currently accepted medical use according to established DEA procedure and case law.

4. *Its history and current pattern of abuse*

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[7]Pursuant to 21 U.S.C. 812(b)(1)(B), when placing a drug or other substance in schedule I, DEA must consider whether the substance has a currently accepted medical use in treatment in the United States. First, DEA looks to whether the drug or substance has FDA approval. When no FDA approval exists, DEA has traditionally applied a five-part test to determine whether a drug or substance has a currently accepted medical use: (1) the drug's chemistry must be known and reproducible; (2) there must be adequate safety studies; (3) there must be adequate and well-controlled studies proving efficacy; (4) the drug must be accepted by qualified experts; and (5) the scientific evidence must be widely available. *See Marijuana Scheduling Petition; Denial of Petition; Remand*, 57 FR 10499 (Mar. 26, 1992), pet. for rev. denied, *Alliance for Cannabis Therapeutics v. Drug Enforcement Admin*., 15 F.3d 1131, 1135 (D.C. Cir. 1994). DEA and HHS applied the traditional five-part test for currently accepted medical use in this matter. In a recent published letter in a different context, HHS applied an additional two-part test to determine currently accepted medical use for substances that do not satisfy the five-part test: (1) whether there exists widespread, current experience with medical use of the substance by licensed health care practitioners operating in accordance with implemented jurisdiction-authorized programs, where medical use is recognized by entities that regulate the practice of medicine, and, if so, (2) whether there exists some credible scientific support for at least one of the medical conditions for which part (1) is satisfied. On April 11, 2024, the Department of Justice's Office of Legal Counsel (OLC) issued an opinion, which, among other things, concluded that HHS' two-part test would be sufficient to establish that a drug has a currently accepted medical use. Office of Legal Counsel, Memorandum for Merrick B. Garland, Attorney General, Re: Questions Related to the Potential Rescheduling of Marijuana at 3 (April 11, 2024). In its eight-factor assessment, HHS determined that tianeptine does satisfy this two-part test. Therefore, because both DEA and HHS have determined that this substance does not satisfy the five-part test, and HHS has determined that this substance does not satisfy the additional two-part test, DEA concludes that tianeptine does not have a currently accepted medical use.

Tianeptine was discovered in the 1960s and patented by the French Society for Medical Research. Tianeptine is currently marketed as a prescription antidepressant in other countries; however, it is not approved for medical use by the FDA within the United States. While still approved for use in various countries, tianeptine has been banned in several localities worldwide due to its opioid-like effects and high potential for misuse. Tianeptine has been banned or classified as a controlled substance in Italy (2020), Turkey (2012), Bahrain (2003), and Russia (2010). Within the United States, internet searches for tianeptine routinely return results for websites offering to sell tianeptine, in addition to various other synthetic drugs, including some schedule I substances. Websites offer language marketing the use of tianeptine as a mood enhancer and to aid in concentration, while suggesting it's safe to use via customer testimonials.

Law enforcement correspondence has reported that users administer tianeptine in a manner similar to heroin (i.e., by injection or nasal insufflation), albeit more frequently due to its shorter duration of action. In addition, while previous studies in rodents failed to report withdrawal symptoms, severe withdrawal symptoms in humans resulting in hospitalization following the use of tianeptine have been reported. According to the Centers for Disease Control and Prevention (CDC), tianeptine is not routinely included in toxicological analysis, and specialized testing may be required to positively identify this substance. This need for specialized analyses may contribute to under reporting of harm and abuse.

Starting in November 2018, FDA issued its first of multiple notices to the public regarding the dangers of tianeptine. Due to various companies and websites selling tianeptine without any labeled warnings as a supplement to improve mental acuity; treat

opioid use disorder, pain, and anxiety; or with no information indicating how or under which conditions to use the product, the FDA felt it was necessary to alert the public of the dangers of ingesting this substance. The full list of alerts can be found in the full eight-factor analysis at *https://www.regulations.gov*, under docket number "DEA1596."

5. *The scope, duration, and significance of abuse*

Amidst the current opioid epidemic, illicit manufacturers and drug traffickers continually look for additional opioid-like substances in order to sell them in the illicit drug market for abuse. Tianeptine is one such substance with opioid-like properties that is not currently controlled under the CSA. In August 2018, the CDC published an analysis of the tianeptine-related calls to the National Poison Data System (NPDS)[8] between 2000 and 2017. According to the CDC, tianeptine-related calls to the poison centers increased markedly from 2014 through 2017. During the first 14 years of the study period (2000-2013), NPDS reported a total of 11 tianeptine exposure calls, whereas 207 calls were reported from 2014 through 2017 (2014 – 5; 2015 – 38; 2016 – 83; 2017 – 81). This rapid and marked increase in calls to poison centers related to tianeptine is an extreme public health concern. The most commonly reported adverse effects among the 21 tianeptine withdrawal-associated calls consisted of: agitation (33.3 percent), nausea (33.3 percent), vomiting (19 percent), tachycardia (19.1 percent), hypertension (14.3 percent), diarrhea (9.5 percent), tremor (9.5 percent), and diaphoresis (9.5 percent). In addition, abrupt cessation of tianeptine may be difficult to tolerate, leading to potentially severe opioid-like withdrawal. In a follow-up study using NPDS data, tianeptine

[8] NPDS is a national database of information provided by the country's regional poison centers serving all 50 states, the District of Columbia, the U.S. Virgin Islands, and Puerto Rico. The American Association of Poison Control Centers maintains the database. NPDS case records are the result of call reports made by members of the public or health care providers. https://www.aapcc.org/data-system/

exposures reported to United States poison centers from 2015 to 2023 increased 1,400 percent from 2015 to 2023, including a 525 percent increase from 2018 to 2023. Most exposures were associated with moderate (51.5 percent) or major (12.0 percent) effects, and 40.1 percent required medical admission, including 22.9 percent to a critical care unit. They also noted that withdrawal accounted for 22.5 percent of tianeptine exposures reported to NPDS (*see* Factor 5 of eight-factor analysis on the docket).

Data collected by the National Forensic Laboratory Information System (NFLIS) reported 268 encounters of tianeptine between March 2017 and February 2026.[9] In one investigation, detectives seized multiple pieces of evidence indicating the presence of tianeptine. Items seized included bulk tianeptine powder (over 1.4 kg), a tableting machine, and over 900 counterfeit pills with various markings for both hydrocodone and oxycodone, found to contain the presence of tianeptine.

As noted in the HHS review, numerous states have controlled or otherwise banned the sale of tianeptine, including Alabama (2021), Arkansas (2022), Florida (2023), Georgia (2024), Indiana (2024), Kentucky (2023), Louisiana (2024), Maryland (2024), Michigan (2018), Minnesota (2023), Mississippi (2023), Ohio (2022), Oklahoma (2019), Tennessee (2022), and Virginia (2024). However, these bans do not prohibit individuals from crossing state lines to buy tianeptine and have not limited the sale and availability of tianeptine online.

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[9] NFLIS represents an important resource in monitoring illicit drug trafficking, including the diversion of legally manufactured pharmaceuticals into illegal markets. NFLIS-Drug is a comprehensive information system that includes data from forensic laboratories that handle more than 96 percent of an estimated 1 million distinct annual federal, state, and local drug analysis cases. NFLIS includes drug chemistry results from completed analyses only. While NFLIS data are not direct evidence of abuse, these can lead to an inference that a drug has been diverted and abused. *See Schedules of Controlled Substances: Placement of Carisoprodol Into Schedule IV,*76 FR 77330, 77332 (Dec. 12, 2011). NFLIS data were queried on February 26, 2026 (2025 and 2026 results still being reported).

Using a variety of databases, HHS found that more patients sought tianeptine for perceived therapeutic purposes than for recreation, with drug withdrawal and dependence being the most frequently reported adverse events. This included a therapeutic effect, such as pain relief, depression or anxiety, or self-detox from another substance, namely opioids. Of note, in the HHS review, the average self-reported maximum dose in one day in this case series was 1,013 mg, with the highest maximum daily reported dose of 63,720 mg in an FDA Adverse Event Reporting System report. This data supports the notion that tianeptine is being taken in significantly higher amounts than is prescribed in other countries for use as an antidepressant.

6. *What, if any, risk there is to the public health*

Available evidence on the overall public health risks associated with the use of tianeptine demonstrate serious health problems leading to emergency department admissions and death. As described in Factor 5, studies using data from the NDPS demonstrated a variety of severe adverse effects, including agitation, nausea/vomiting, and tachycardia, among many others. Data from overdose reports also demonstrates that tianeptine is being abused in combination with other substances. Case reports detailing serious adverse effects have been reported in the literature (*see* additional cases at *www.regulations.gov* contained within DEA's eight-factor analysis at docket DEA-1596). Some examples of the risk to public health include the following:

a. A 36-year-old male in Virginia intentionally injected intravenously (IV) tianeptine powder dissolved in water. He became unresponsive and a bystander called emergency medical services. He was administered naloxone 1 mg IV onsite before being transported to the emergency department. Upon arrival, he had excessive constriction of

the pupils, sedation, and a respiratory rate of 6 respirations per minute. His toxicity was successfully reversed with two doses of naloxone 0.4 mg IV, and he was placed on naloxone infusion at 0.2 mg/hour. Urine toxicology results were negative for common drugs of abuse and tricyclic antidepressants but were positive for ethanol and tianeptine.

b. A 42-year-old male in New York displayed shallow and variable breathing and was unresponsive to attempts for arousal. He was administered 0.8 mg of naloxone in the ambulance leading to arousal and improved respiration. A second dose of naloxone resulted in improved alertness and spontaneous respirations. Toxicology was positive for tianeptine and alprazolam. He reported discovering tianeptine from internet blogs and was able to purchase it online. The patient noted that tianeptine induced euphoria and a "sense of calm" following "one scoop" of powder. He noted the effects were short lived and reported tolerance needing larger doses over time to achieve the same desired effects.

c. Two overdose death cases involving tianeptine were identified in Texas. A 28-year-old male with a history of illicit drug use was found dead on the floor of his locked residence. Autopsy findings included pulmonary edema, modest cardiomegaly, and urinary retention. Toxicology was positive for tianeptine and a presumptive positive for 7-aminoclonazolam. In a second unrelated case, a 30-year-old male was found dead in his secure residence. He had a history involving a head injury (9 years prior) and was being treated with alprazolam for anxiety and paranoia. The decedent had purchased tianeptine powder and needles for injection via the internet. Evidence of hypertensive cardiovascular disease, pulmonary edema, and pulmonary congestion were noted upon autopsy. Toxicology was positive for tianeptine and alprazolam.

d. A 49-year-old male in Pennsylvania was found deceased in his bedroom. A digital scale with a white powdery substance and other paraphernalia were located on the nightstand next to the bed. Following a full toxicology panel for the decedent, the coroner listed the cause of death as tianeptine toxicity.

The abuse of tianeptine, as demonstrated above, has resulted in severe adverse reactions to include respiratory depression, severe sedation, and death. Reversal of overdose toxicity of tianeptine by the opioid antagonist naloxone in multiple scenarios suggests the involvement of the opioid receptors' mechanisms in tianeptine toxicity.

7. *Its psychic or physiological dependence liability*

As described previously, tianeptine has a similar mechanism of action and adverse side effects to other mu-opioid agonists. In addition, cessation of tianeptine use can lead to withdrawal symptoms similar to other opioid-withdrawal effects. HHS described multiple cases in their review regarding both dependence and withdrawal following the use of tianeptine. A case report noted that tianeptine has been used to self-treat opioid withdrawal but can cause its own dependence and withdrawal with prolonged use. In addition, the case reports described earlier have also demonstrated withdrawal symptoms and tolerance associated with the abuse of tianeptine. In a review cited by HHS, study authors reviewed an additional 18 case reports from the scientific literature and concluded that, in addition to marked euphoria, withdrawal symptoms perpetuating further drug misuse were the most prominent phenomena associated with tianeptine abuse. The study authors also noted that the amount of tianeptine used exceeded the therapeutic dose in countries where it is legal by approximately 110-fold. Reports of numerous cases of tianeptine misuse or abuse showed withdrawal symptoms consisting

of myalgia, chills, anxiety, excitability, nausea, vomiting, tremor, mood lability, insomnia, rhinorrhea, diarrhea, and cravings. An additional case described a patient with a two-week history of tianeptine use that reported taking 10 to 15 pills daily of an unspecified dosage and needing to take the drug at least every 4 to 6 hours to prevent the onset of symptoms of withdrawal. Collectively, these data demonstrate the similarity of tianeptine and both its mechanism of action and adverse side effects to other mu-opioid agonists, including the precipitation of withdrawal symptoms following the cessation of its use.

8. *Whether the substance is an immediate precursor of a substance already controlled under this subchapter*

Tianeptine is not an immediate precursor of any substance controlled under the CSA, as defined in 21 U.S.C. 802(23).

Conclusion:

After considering the scientific and medical evaluation conducted by HHS, the accompanying recommendation of HHS, and DEA's own eight-factor analysis, DEA finds that the facts and all relevant data constitute substantial evidence of the potential for abuse of tianeptine. As such, DEA hereby proposes to permanently schedule tianeptine as a schedule I controlled substance under the CSA.

Proposed Determination of Appropriate Schedule

The CSA establishes five schedules of controlled substances known as schedules I, II, III, IV, and V. The CSA also outlines the findings required to place a drug or other substance in any particular schedule.[10] After consideration of the analysis and

[10] 21 U.S.C. 812(b).

recommendation of the Assistant Secretary for Health of HHS and review of all other available data, the Administrator of DEA, pursuant to 21 U.S.C. 811(a) and 812(b)(1), finds that:

1. Tianeptine has a high potential for abuse

Tianeptine has been shown to be pharmacologically similar to other mu-opioid agonists, including morphine (schedule II) and fentanyl (schedule II). In addition, epidemiological data and case reports demonstrate that the adverse effect profile of tianeptine is similar to other opioids. Users are ingesting tianeptine in high dosages for its opioid effects, resulting in serious harm, including fatal overdoses both in combination with other opioids and with tianeptine alone. HHS has concluded that tianeptine has a high potential for abuse.

2. Tianeptine has no currently accepted medical use in treatment in the United States

According to HHS, FDA has not approved a marketing application for tianeptine for any therapeutic indication. In addition, there is a lack of support among medical experts in the United States and from clinical studies to consider tianeptine an acceptable medicine in the United States for any medical uses, nor are there any state-authorized programs that permit the medical use of tianeptine. For these reasons, FDA concluded that tianeptine has no currently accepted medical use in treatment in the United States.

3. There is a lack of accepted safety for use of tianeptine under medical supervision

As stated by HHS, tianeptine has no approved medical use and has not been thoroughly investigated as a new drug in the United States. Therefore, the safety of

tianeptine for use under medical supervision has not been determined. Thus, there is a lack of accepted safety for the use of tianeptine under medical supervision.

Based on these findings, the Administrator concludes that tianeptine (7-[(3-chloro-6,11-dihydro-6-methyl-5,5-dioxidodibenzo[*c,f*][1,2]thiazepin-11-yl)amino]heptanoic acid), including its isomers, esters, ethers, salts, and salts of isomers, esters, and ethers, warrants control in schedule I of the CSA. More precisely, because of its depressant-like effects, DEA is proposing to place tianeptine in 21 CFR 1308.11(b) (the opioids category of schedule I).

Requirements for Handling Tianeptine

If this rule is finalized as proposed, tianeptine would be subject to the CSA's schedule I regulatory controls and administrative, civil, and criminal sanctions applicable to the manufacture, distribution, reverse distribution, dispensing, import, export, engagement in research, conduct of instructional activities or chemical analysis with, and possession of schedule I controlled substances, including the following:

1. Registration. Any person who handles (manufactures, distributes, dispenses, imports, exports, engages in research, or conducts instructional activities or chemical analysis with, or possesses), or who desires to handle, tianeptine would need to be registered with DEA to conduct such activities pursuant to 21 U.S.C. 822, 823, 957, and 958, and in accordance with 21 CFR parts 1301 and 1312.

Any person who currently handles tianeptine and is not registered with DEA to conduct research with a schedule I controlled substance must submit an application for registration and may not continue to handle tianeptine, unless DEA has approved that

application for registration pursuant to 21 U.S.C. 822, 823, 957, 958, and in accordance with 21 CFR parts 1301 and 1312.

Notwithstanding the foregoing, pursuant to 21 U.S.C. 822(h), if, on the date the final rule is effectuated, a person is conducting research on tianeptine and is already registered to conduct research with another controlled substance in schedule I, the person may continue to conduct research on tianeptine if they submit a completed application for registration or modification of existing registration, as applicable, to conduct research with tianeptine not later than 90 calendar days after the date of effectuation of the final rule. The person may continue to conduct such research until the person withdraws the application or the Administrator serves on the person an order to show cause proposing denial of the application pursuant to 21 U.S.C. 824(c) and in accordance with 21 CFR 1301.37. If the Administrator serves an order to show cause proposing denial of the application or modification, the person may not continue to conduct research with tianeptine and may not receive or otherwise obtain additional tianeptine. If an order to show cause is served and the person requests a hearing in accordance with 21 CFR 1301.37(d), the hearing shall be held in accordance with 21 CFR 1301.41-1301.46 on an expedited basis and not later than 45 calendar days after the request is made, except that the hearing may be held at a later time if so requested by the person. If the person sends a copy of the application to a manufacturer or distributor of tianeptine, receipt of the copy by the manufacturer or distributor constitutes sufficient evidence that the person is authorized to receive tianeptine pursuant to 21 U.S.C. 822(h)(4). Continuation of research under 21 U.S.C. 822(h) does not authorize any other handling (e.g., distribution) of tianeptine.

Retail sales of schedule I controlled substances to the general public are not allowed under the CSA. Possession of any quantity in a manner not authorized by the CSA is unlawful, and those in possession of any quantity may be subject to prosecution pursuant to the CSA.

2. Disposal of Stocks. Any person unwilling or unable to obtain a schedule I registration must surrender or transfer all quantities of currently held tianeptine to a person registered with DEA before the effective date of the final scheduling action in accordance with all applicable Federal, State, local, and Tribal laws. Tianeptine must be disposed of in accordance with 21 CFR part 1317, in addition to all other applicable Federal, State, local, and Tribal laws.

3. Security. Tianeptine would be subject to schedule I security requirements and must be handled and stored pursuant to 21 U.S.C. 821, 823, and in accordance with 21 CFR 1301.71–1301.76. Non-practitioners handling tianeptine also would need to comply with the screening requirements of 21 CFR 1301.90–1301.93.

4. Labeling and Packaging. All labels and labeling for commercial containers of tianeptine would need to comply with 21 U.S.C. 825 and 958(e), and be in accordance with 21 CFR part 1302.

5. Quota. Generally, only registered manufacturers would be permitted to manufacture tianeptine in accordance with a quota assigned, pursuant to 21 U.S.C. 826, and in accordance with 21 CFR part 1303.

6. Inventory. Every DEA registrant who would handle tianeptine must have an initial inventory of all stocks of controlled substances (including this substance) on hand on the date the registrant first engages in the handling of controlled substances pursuant

to 21 U.S.C. 827 and 958, and in accordance with 21 CFR 1304.03, 1304.04, and 1304.11.

After the initial inventory, every DEA registrant would need to take a new inventory of all stocks of controlled substances (including tianeptine) on hand every two years pursuant to 21 U.S.C. 827 and 958(e), and in accordance with 21 CFR 1304.03, 1304.04, and 1304.11.

7. Records and Reports. Every DEA registrant would need to maintain records and submit reports with respect to tianeptine, pursuant to 21 U.S.C. 827, 832(a), and 958(e), and in accordance with 21 CFR 1301.74 and 1301.76, and parts 1304, 1312, and 1317. Manufacturers and distributors would need to submit reports regarding tianeptine to the Automation of Reports and Consolidated Order System pursuant 21 U.S.C. 827, and in accordance with 21 CFR parts 1304 and 1312.

8. Order Forms. Every DEA registrant who distributes tianeptine would need to comply with the order form requirements, pursuant to 21 U.S.C. 828 and 21 CFR part 1305.

9. Importation and Exportation. All importation and exportation of tianeptine would need to comply with 21 U.S.C. 952, 953, 957, and 958, and in accordance with 21 CFR part 1312.

10. Liability. Any activity involving tianeptine not authorized by, or in violation of, the CSA or its implementing regulations would be unlawful, and may subject the person to administrative, civil, and/or criminal sanctions.

Regulatory Analyses

Executive Orders 12866, 13563, 14192, and 14294

In accordance with 21 U.S.C. 811(a), this proposed scheduling action is subject to formal rulemaking procedures done "on the record after opportunity for a hearing," which are conducted pursuant to the provisions of 5 U.S.C. 556 and 557. The CSA sets forth the criteria for scheduling a drug or other substance. Such actions are exempt from review by the Office of Management and Budget (OMB) pursuant to section 3(d)(1) of Executive Order (E.O.) 12866 and the principles reaffirmed in E.O. 13563. DEA scheduling actions are not subject to either E.O. 14192, Unleashing Prosperity Through Deregulation, or E.O. 14294, Fighting Overcriminalization in Federal Regulations.

Executive Order 12988, Civil Justice Reform

This proposed regulation meets the applicable standards set forth in sections 3(a) and 3(b)(2) of E.O. 12988 to eliminate drafting errors and ambiguity, minimize litigation, provide a clear legal standard for affected conduct, and promote simplification and burden reduction.

Executive Order 13132, Federalism

This proposed rulemaking does not have federalism implications warranting the application of E.O. 13132. The proposed rule does not have substantial direct effects on the States, on the relationship between the National Government and the States, or the distribution of power and responsibilities among the various levels of government.

Executive Order 13175, Consultation and Coordination with Indian Tribal Governments

This proposed rule does not have Tribal implications warranting the application of E.O. 13175. It does not have substantial direct effects on one or more Indian tribes, on the relationship between the Federal Government and Indian tribes, or on the distribution of power and responsibilities between the Federal Government and Indian tribes.

Regulatory Flexibility Act

The Administrator, in accordance with the Regulatory Flexibility Act, 5 U.S.C. 601–602, has reviewed this proposed rule and, by approving it, certifies that it will not have a significant economic impact on a substantial number of small entities.

According to HHS, tianeptine has a high potential for abuse, has no currently accepted medical use in treatment in the United States, and lacks accepted safety for use under medical supervision. There appear to be no legitimate sources for tianeptine as a marketed drug in the United States, but DEA notes that this substance is available for purchase from legitimate suppliers for scientific research. There is no evidence of significant diversion of tianeptine from legitimate suppliers. Therefore, DEA has concluded that this proposed rule, if finalized, will not have a significant economic impact on a substantial number of small entities.

The entities affected by this proposed rule include the manufacturers, distributors, importers, exporters, and researchers of tianeptine. DEA determines the North American Industry Classification System (NAICS) industries that best represent these business activities. Table 1 lists the business activities and corresponding NAICS industries.[11]

Table 1: Business Activity and Corresponding NAICS Industries.

Business Activity	NAICS Code	NAICS Industry Description
Manufacturer	325412	Pharmaceutical Preparation Manufacturing
Distributor, Importer, Exporter	424210 424690	Drugs and Druggists' Sundries Merchant Wholesalers Other Chemical and Allied Products Merchant Wholesalers
Researcher	541715 611310	Research and Development in Physical, Engineering, and Life Sciences (except Nanotechnology and Biotechnology) Colleges, Universities and Professional Schools

[11] Executive Office of the President Office of Management and Budget, North American Industry Classification System, United States, 2022, https://www.census.gov/naics/reference_files_tools/2022_NAICS_Manual.pdf. (Accessed 9/25/2025.)

From Statistics of United States Businesses (SUSB) data, DEA determined the number of firms and small firms for each of the affected industries, and by comparing the number of affected small entities to the number of small entities for each industry, DEA determined whether a substantial number of small entities are affected in any of the industries. Table 2 lists the number of firms, small firms, and percent small firms in each affected industry.

Table 2: Percent Affected Small Entities by Industry.

NAICS Industry	Firms[12]	SBA Size Standard[13]	Small Firms[14]	Percent of Small Entities (percent)
325412-Pharmaceutical Preparation Manufacturing	1,179	1,300 employees	1,099	93.2
424210-Drugs and Druggists' Sundries Merchant Wholesalers	7,012	250 employees	6,760	96.4
424690-Other Chemical and Allied Products Merchant Wholesalers	5,487	175 employees	5,197	94.7
541715-Research and Development in the Physical, Engineering, and Life Sciences (except Nanotechnology and Biotechnology)	10,042	1,000 employees	9,599	95.6
611310-Colleges, Universities and Professional Schools	2,494	$34.5 million	1,515	60.8

Based on the American Chemical Society's SciFinder database,[15] DEA identified 26 entities supplying tianeptine across the industries 325412, 424210, and 424690.

[12] Statistics of U.S. Businesses, 2022 SUSB Annual Data Tables by Establishment Industry, https://www.census.gov/data/tables/2021/econ/susb/2021-susb-annual.html (Accessed 9/25/2025)
[13] U.S. Small Business Administration, Table of size standards, Version March 2023, Effective: March 17, 2023, https://www.sba.gov/sites/default/files/2023-06/Table%20of%20Size%20Standards_Effective%20March%2017%2C%202023%20%282%29.pdf (accessed September 25, 2025)
[14] Based on the estimated number of firms below the SBA size standard for each industry.
[15] SciFinder; Chemical Abstracts Service: Columbus, OH; CAS 2504100-70-1; https://scifinder.cas.org (accessed September 24, 2025).

However, one entity has already registered with DEA to handle controlled substances. Hence, DEA expects 25 of the entities in the 325412, 424210, and 424690 industries will be affected by this rule. Assuming that all affected suppliers were small entities and concentrated in the smallest NAICS industry, 325412-Pharmaceutical Preparation Manufacturing, they would account for insubstantial number of small entities in that industry, 2.27 percent.[16]

Additionally, DEA expects that the number of researchers working with tianeptine is small, because tianeptine is not approved for medical use and has a substantial capability to be a hazard to the health of the user and to the safety of the community. Also, DEA believes that the researchers working with tianeptine may also work with other controlled substances; hence, these researchers are likely already registered with DEA and are qualified to handle controlled substances. For these reasons, DEA believes the number of affected researchers that are small entities is not a substantial number of small entities in 541715 and 611310 industries.

In summary, the small entities affected by this proposed rule are those in 325412-Pharmaceutical Preparation Manufacturing, 424210-Drugs and Druggists' Sundries Merchant Wholesalers, and 424690-Other Chemical and Allied Products Merchant Wholesalers. The affected small entities account for less than 2.27 percent of the small businesses and are not likely to manufacture or carry inventory of tianeptine. As such, the proposed rule, if finalized, is not expected to result in a significant economic impact on a substantial number of small entities.

Unfunded Mandates Reform Act of 1995

[16] 25/1,099 = 2.27 percent.

In accordance with the Unfunded Mandates Reform Act (UMRA) of 1995, 2 U.S.C. 1532*,* DEA has determined and certifies that this action would not result in any Federal mandate that may result "in the expenditure by State, local, and Tribal governments, in the aggregate, or by the private sector, of $100,000,000 or more (adjusted annually for inflation) in any 1 year . . . ." Therefore, neither a Small Government Agency Plan nor any other action is required under UMRA of 1995.

Paperwork Reduction Act of 1995

This proposed rule would require compliance with the following existing OMB collections: 1117-0003, 1117-0004, 1117-0006, 1117-0008, 1117-0009, 1117-0010, 1117-0012, 1117-0014, 1117-0021, and 1117-0056. An agency may not conduct or sponsor, and a person is not required to respond to a collection of information unless it displays a currently valid OMB control number.

List of Subjects in 21 CFR Part 1308

Administrative practice and procedure, Drug traffic control, Reporting and recordkeeping requirements.

For the reasons set out above, DEA proposes to amend 21 CFR part 1308 as follows:

PART 1308—SCHEDULES OF CONTROLLED SUBSTANCES

1. The authority citation for part 1308 continues to read as follows:

Authority: 21 U.S.C. 811, 812, 871(b), 956(b), unless otherwise noted.

2. In § 1308.11:

a. Add new paragraph (b)(117);

b. Redesignate paragraphs (b)(117) through (121) as (b)(118) through (122);

§ 1308.11 Schedule I.

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(d) * * *

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(117) Tianeptine (other name: 7-[(3-chloro-6,11-dihydro-6-methyl-5,5-dioxidodibenzo[c,f][1,2]thiazepin-11-yl)amino]heptanoic acid)	9640
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SIGNING AUTHORITY

This document of the Drug Enforcement Administration was signed on July 6, 2026, by Administrator Terrance Cole. That document with the original signature and date is maintained by DEA. For administrative purposes only, and in compliance with requirements of the Office of the Federal Register, the undersigned DEA Federal Register Liaison Officer has been authorized to sign and submit the document in electronic format for publication, as an official document of DEA. This administrative process in no way alters the legal effect of this document upon publication in the *Federal Register*.

Leslie Mayer,
Federal Register Liaison Officer,
Drug Enforcement Administration.

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