Tianeptine Product Adverse Event Reports from the FDA CFSAN Adverse Event Reporting System (CAERS), 2015 – 2022

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Abstract

Tianeptine is an antidepressant drug used in some European, Asian, and Latin American countries but it is not approved for any use by the U.S. Food and Drug Administration (FDA). In 2018 and 2022, FDA alerted consumers about tianeptine being used as an ingredient in products marketed as dietary supplements stating that tianeptine is a substance that does not meet the statutory definition of a dietary ingredient and is an unsafe food additive. The alert also provided information about the safety risk of tianeptine use. Even with FDA warnings, vendors continue to market and sell these products under a variety of names (e.g. Tianaa, Tianeptine sulfate, ZaZa Red, and Pegasus).

The FDA Center for Food Safety and Applied Nutrition (CFSAN) Adverse Event Reporting System (CAERS) is a post-market surveillance system that receives and monitors adverse event (AE) and product complaint (PC) reports for foods, dietary supplements, and cosmetics. CAERS has received a total of 35 reports involving tianeptine products since 2015. In 2022 alone, CAERS received more reports than the previous three years combined, with 15 reports.

Analysis of the 35 reports revealed that the age of those reporting tianeptine product use ranges from 22 to 57 years old with most reporters being male (83%). The adverse events reported following tianeptine use included anxiety, cardiac disorder, dependence, depression, nausea, and withdrawal. The CAERS reports concerning tianeptine mentioned outcomes of death (2), hospitalizations or healthcare sought (11), life threatening situations (14), and other serious outcomes. Of the 35 reports, 27 (77%) included psychiatric disorders in the reported Medical Dictionary for Regulatory Activities (MedDRA) System Organ Classes (SOCs).

Tianeptine is not approved for any medical use, or as a food additive, is not generally recognized as safe and does not qualify as a dietary ingredient. Consumption of these products can result in serious health outcomes. CAERS provides a vital surveillance role while FDA continues to monitor these products and take regulatory actions to protect the public from unapproved tianeptine products.

Introduction

FDA considers tianeptine to be a substance that does not meet the statutory definition of a dietary ingredient and is an unsafe food additive. Because tianeptine does not qualify as a dietary ingredient, is not an approved food additive, and is not GRAS, any dietary supplements containing tianeptine are adulterated under the FD&C Act. Tianeptine is used as a prescription drug in some European, Asian, and Latin American countries, but it is not approved as a drug in the U.S.

Consumers may inadvertently find themselves addicted to tianeptine. FDA advises the public to avoid all products containing tianeptine, especially those claiming to treat opioid use disorder (OUD). Consumer warnings and information on the risk of using products with tianeptine were issued in 2018 and 2022.

The FDA is aware of several serious adverse event reports associated with tianeptine. CAERS provides a venue to report adverse events (AEs) and product complaints (PCs) pertaining to products marketed as foods, dietary supplements, and cosmetics. The purpose of CAERS is to facilitate consumer protection through real-time assessment of AE reports and provide a database for signal detection analyses.

Materials and Methods

CAERS receives AE reports via a variety of sources including MedWatch, Safety Reporting Portal (SRP), Field Accomplishments and Compliance Tracking System (FACTS), emails, and telephone calls. AEs are coded to terms in the Medical Dictionary for Regulatory Activities (MedDRA). A single CAERS AE report can have more than one type of outcome.

The CAERS database was queried for reports containing "tianeptine" in products and ingredients. Table 1 shows all of the product names associated with tianeptine.

The data extracted included the CAERS ID, age, sex, outcomes, symptoms, CFSAN product type, and System Organ Classes (SOCs). The data from the reports were assessed and analyzed to provide further information.

Table 1. Tianeptine product names and ingredients used in CAERS database query and the number of reports associated with each product/ingredient.

Product/Ingredient	Number of CAERS Reports[3]
KNB Organics	1
Pegasus	2
TD Plus	1
TD Red	1
Tianaa	5
Tianeptine	3
Tianeptine Sodium	5
Tianeptine Sulfate	1
Tianna	7
Za Za	12

[3]More than one product/ingredient may have been reported in a single CAERS report.

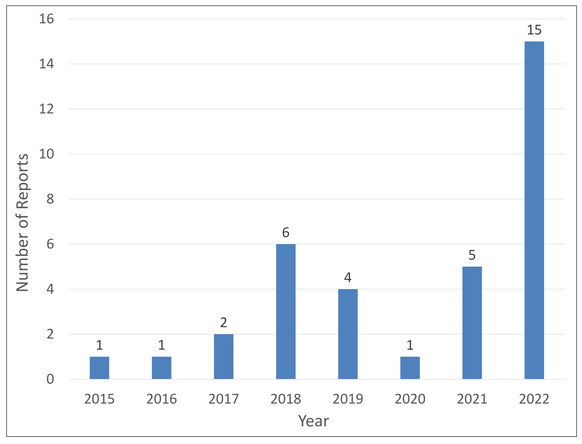

Figure 1. CAERS tianeptine reports by year

Results and Discussion

Starting in 2015, CAERS began receiving AE reports involving tianeptine. From 2015 through 2022, 35 AE reports were submitted to CAERS. All of these reports related to products marketed as dietary supplements and all of the reports were submitted by consumers. Figure 1 shows the number of reports related to tianeptine received each year.

Of the 35 reports, most (83%) were submitted by males. The age of those submitting reports ranged from age 22 to 57. Figures 2 and 3 show the sex and age breakdown of those submitting reports.

Many consumers did not state a reason for why they used products containing tianeptine but they did note that the products were marketed as an "energy aid," "mood stabilizer," or "pain reliever." Once taken, consumers reported opioid addiction-like symptoms and outcomes. Two deaths were reported to CAERS as a result of tianeptine use. Figures 4 and 5 show the symptoms and outcomes reported by consumers.

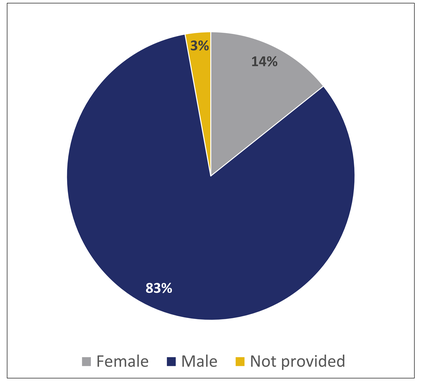

Figure 2. Sex of consumers reporting tianeptine use

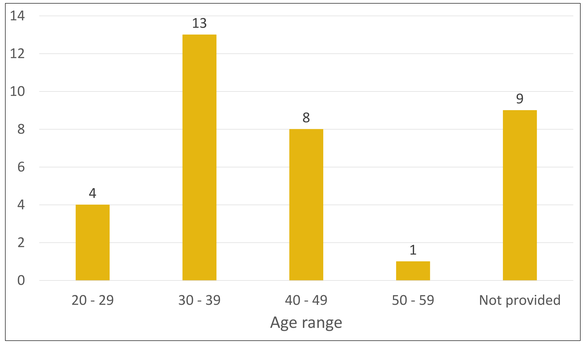

Figure 3. Age range of consumers reporting tianeptine use

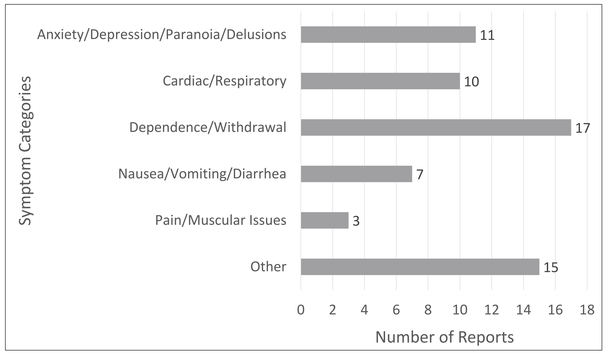

Figure 4. Symptoms reported by consumers from using products with tianeptine.

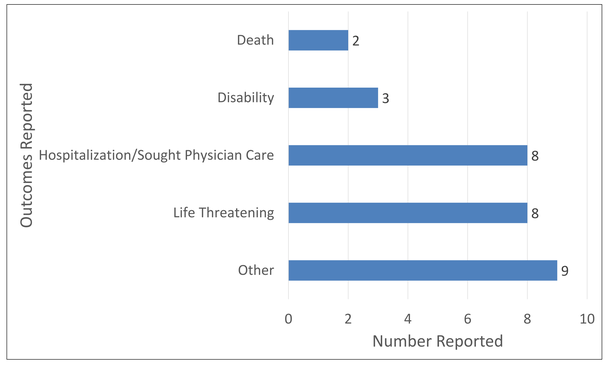

Figure 5. Outcomes reported by consumers using products with tianeptine.

Conclusion

- Tianeptine is not approved for any medical use or as a food additive
- These products remain a public health concern
- CAERS is an essential surveillance and monitoring tool for products that contain tianeptine
- FDA has already taken steps to protect consumers and will continue to take regulatory action to discourage importation and marketing of these products