

Tianeptine

Tianeptine is an atypical tricyclic antidepressant used in Europe, Asia and Latin America. It has antidepressant and anxiolytic properties. While its structure is similar to that of tricyclic antidepressants, its pharmacologic profile is different. Tianeptine enhances serotonin reuptake and modulates neuroplasticity in the hippocampus, amygdala and prefrontal cortex. As tianeptine is also a mu opioid receptor agonist, there is concern about its potential for abuse.

Tianeptine is not approved by the Food and Drug Administration (FDA) for use in the U.S. but is available online as a research chemical or as a dietary supplement or cognitive enhancer. Since the FDA has not approved it for any use, dietary supplements containing tianeptine are considered adulterated with an unsafe food additive. Unproven claims that it can treat opioid use disorder, pain, stress, and other ailments are illegal. In November 2018 the FDA posted warning letters to two companies for illegal marketing of tianeptine-containing dietary supplements (<https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm626349.htm>).

Case reports of tianeptine misuse and abuse describe similar effects as opioids and use of naloxone with positive response. Acute toxic effects include agitation, sedation, respiratory depression, miosis and arrhythmias. A literature review conducted in 2018 found 25 articles involving 65 patients with tianeptine abuse or dependence (*Psychosomatics*. July 19, 2018; E-pub ahead of print). The majority of cases (53) were outside the U.S. Three quarters of patients were male and under the age of 35 years. The average daily dose was close to 2 grams, far above the usual therapeutic dose of 25-50 mg daily. Routes of administration included oral, intravenous and insufflation. There were 9 deaths, three of which involved at least one other substance. Another 2018 literature review of 18 patients observed a prior history of substance abuse in 72%. Doses were well above therapeutic with a mean of 1469 mg/day and as high as 4125 mg/day (*J Psychoactive Drugs* 2018;50:275-80). The Centers for Disease Control and Prevention (CDC) analyzed 218 tianeptine exposure calls reported to poison control centers in the U.S. from 2000 to 2017 (*MMWR* 2018;67:815-8). From 2000 to 2013 there were only 11 calls; the increase in calls and in intentional abuse or misuse from 2014-2017 was statistically significant. The mean age was 35 years with the majority of cases involving persons 21-40 years. Most common clinical effects in the 114 tianeptine-only exposures (excluding withdrawal related calls) were neurologic (48%), cardiovascular (32.5%) and gastrointestinal (10.5%). The most common co-exposures in 83 patients with other substances were phenibut, ethanol, benzodiazepines and opioids.

Chronic tianeptine users develop dependence and withdrawal symptoms that are similar to those of opioid withdrawal. In the CDC study referenced above, there were 21 tianeptine-only withdrawal calls to poison centers. The most frequently reported effects in these patients were agitation, nausea, vomiting, tachycardia, hypertension, diarrhea, tremor and diaphoresis.



Did you know?

Anyone can submit a report regarding product safety concerns.

The FDA and National Institutes of Health (NIH) have an on-line Safety Reporting Portal for issues regarding food, medicines, dietary supplements, and other products. Some organizations and professionals are required by law to submit reports. Health care providers, other professionals and consumers/concerned citizens may voluntarily submit reports regarding safety and/or unanticipated harmful effects of products. Use this link for reporting: <https://www.safetyreporting.hhs.gov>.

Wendy Klein-Schwartz, PharmD, MPH, FAACT
Professor Emeritus
University of Maryland School of Pharmacy



@MPCToxTidbits