March Pharmacy Newsletter

What is the Black Box Warning on Trazodone?

The Food and Drug Administration (FDA) has issued a black box warning for trazodone. A black box warning is used to inform consumers about dangerous potential effects of a prescription drug. According to trazodone label, it can produce or increase suicidal thoughts in children and young adults.

Trazodone is a generic drug prescribed to treat depression and more often used off label for the treatment of insomnia. Possible serious side effects of trazodone include rapid heart rate, visual disturbances and increased suicidal thoughts.

Trazodone warnings include serotonin syndrome, which include symptoms of agitation, hallucinations, confusion, or trouble thinking, nausea, vomiting, and diarrhea. Other issues include coordination disturbance, muscle twitching, stiff muscles, racing heart rate, high or low blood pressure, sweating, fever, and coma. Taking trazodone with drugs, such as citalopram, fluoxetine, paroxetine, sertraline, venlafaxine, duloxetine, and St. John's wort may increase the risk of serotonin syndrome. This condition can be life threatening.

Trazodone may cause pupils to be slightly bigger and lead to angle-closure glaucoma (a condition that causes increased pressure in eyes). Avoid use of antidepressants, including trazodone hydrochloride, in patients with untreated anatomically narrow angles.

Taking trazodone with warfarin, dabigatran, rivaroxaban, and pain medications like nonsteroidal anti-inflammatory drugs (NSAIDs), such as ibuprofen and aspirin may increase risk for bleeding.

There is a higher risk for manic episodes in patients with a history of mania or bipolar disorder. While antidepressants can help relieve symptoms of depression, they do not help with bouts of mania. For this reason, antidepressants are not always the most effective treatment for people with bipolar disorder.

Using trazodone for insomnia can be effective for short term treatment. The off-label dosage is 50mg to 100mg -1 hour prior to bedtime but generally sleeping pills are not the best long-term treatment for insomnia. A safer and more effective treatment for long-term sleep problems like insomnia is cognitive behavioral therapy (CBT). Generally, it is the first treatment recommended.

An aside note, trazodone is one of the medications included in the HEDIS measure AMM-Antidepressant Medications Measure that evaluates percentage of members 18 years of age and older who were treated with antidepressant medication, had a diagnosis of major depression and who remained on an antidepressant medication treatment for the continuation phase. The insomnia dosing is not excluded, therefore affecting the possibility of meeting the metric measurement, due to trazodone being used short term for insomnia and not meeting continuity of treatment, per the measurement definition.

The two rates reported are:
Effective Acute Phase Treatment: Adults who remained on an antidepressant medication for at least 84 days (12 weeks).
Effective Continuation Phase Treatment: Adults who remained on an antidepressant medication for at least 180 days (6 months).

****Meds approved by NCQA for HEDIS:**

AMM - Meds**	Antidepressant Medications
	• **Miscellaneous antidepressants:** Bupropion, Vilazodone, Vortioxetine • **Monoamine oxidase inhibitors:** Isocarboxazid, Phenelzine, Selegiline, Tranylcypromine • **Phenylpiperazine antidepressants:** Nefazodone, Trazodone • **Psychotherapeutic combinations:** Amitriptyline-chlordiazepoxide, Amitriptyline-perphenazine, Fluoxetine-olanzapine • **SNRI antidepressants:** Desvenlafaxine, Duloxetine, Levomilnacipran, Venlafaxine • **SSRI antidepressants:** Citalopram, Escitalopram, Fluoxetine, Fluvoxamine, Paroxetine, Sertraline • **Tetracyclic antidepressants:** Maprotiline, Mirtazapine • **Tricyclic antidepressants:** Amitriptyline, Amoxapine, Clomipramine, Desipramine, Doxepin (>6mg), Imipramine, Nortriptyline, Protriptyline, Trimipramine

"Gas Station Heroin" - A growing Concern Over Dietary Supplement, Tianeptine

The FDA has issued a consumer warning to avoid products containing tianeptine. Tianeptine, sold under brand names Stablon, Coaxil and Tatinol, is used for treatment resistant depression in European, Latin American, and Asian countries. The illicit substance can be found in bulk powder, counterfeit pills mimicking hydrocodone, and individual stamp bags, used to distribute heroin. The pharmacological structure of the compound acts as a mu opioid agonist and is most often encountered in salt form. Health officials in Florida, Alabama, Georgia, Indiana, Kentucky, Michigan, Mississippi, Ohio, and Tennessee have banned tianeptine after warning from public health officials.

Tianeptine, often referred to as "gas station heroin" due the popularity of the product found in gas stations, convenience stores and smoke shops. According to lawmakers, the product is extremely addictive due to euphoric properties mimicking heroin. The United States Food and Drug Administration issued caution against products containing Tianeptine, such as Neptune's Fix, Za Za Red, and Tianaa. These products are illegally sold with descriptions like "happiness in a bottle" and claim to improve cognition, treat anxiety, depression, and pain. A "Neptune's Fix" recall was issued due to "reasonable probability of life- threatening events including suicidal ideation or behavior in children, adolescents and young adults." In addition to tianeptine, product samples of the brand were found to contain synthetic cannabinoids, commonly associated with severe and life-threatening health complications. Hospitalizations following withdrawal symptoms have been reported with evidence of severe adverse respiratory, cardiovascular, gastrointestinal, and neurological complications. As of Jan. 1, 2024, the FDA issued a letter to retailers to stop selling Neptune's Fix and any other tianeptine-containing products.

With a growing online presence and ease of access, it is important to educate consumers on the importance of using FDA approved products. Convenience stores, gas stations, and online retailers can be appealing with reasonably priced products promising results in treating anxiety, depression, pain, and improving brain function. Consumers should speak to their provider or pharmacist before starting over-the-counter medication to avoid drug or disease state interactions. Healthcare professionals and consumers can report side effects related to tianeptine or any other product to the FDA's MedWatch Safety Information and Adverse Event Reporting Program

References:

1. https://www.accessdata.fda.gov/drugsatfda_docs/label/2015/071196s062lbl.pdf
2. https://www.drugs.com/pro/trazodone.html

3. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6269438/
4. https://www.mayoclinic.org/diseases-conditions/insomnia/in-depth/insomnia-treatment/art-20046677
5. https://www. fda.gov/drugs/drug-safety-and-availability/fda-warns-consumers-not-purchase-or-use-neptunes-fix-or-any-tianeptine-product-due-serious-risks
6. https://www.deadiversion.usdoj.gov/drug_chem_info/tianeptine.pdf
7. https://www.wsaz.com/2024/01/22/lawmakers-urge-fda-review-gas-station-heroin/

REFERRED DRUG LIST UPDATES CAN BE FOUND HERE:

Integrated (Title 19/21 SMI), ACC, DD, ALTCS and DCS CHP
https://www.mercycareaz.org/providers/pharmacy.html

Behavioral Health (Non-Title 19/21)
https://www.mercycareaz.org/providers/pharmacy.html

** Drugs that are not on the formulary will require a PA (prior authorization) request to be submitted**

Reminder for quicker determinations of a Prior Authorization use the ePA link for Our Providers: Please click here to initiate an electronic prior authorization (ePA) request

This newsletter is brought to you by the Mercy Care Pharmacy Team. For questions, please email Fanny A Musto (MustoF@mercycareaz.org), Denise Volkov (VolkovD@mercycareaz.org) or Trennette Gilbert (gilbert@mercycareaz.org)