ToxTalks:

A Bulletin for Healthcare Professionals Who Manage Poisoned Patients

In Partnership with the UVA Division of Medical Toxicology – Department of Emergency Medicine

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Phenibut

Background

Phenibut was first synthesized at the USSR Academy of Medical Science and introduced for clinical use in Russia in the 1960s. It was reported to have beneficial effects to reduce anxiety, improve sleep quality, and help depression. The medication has not been approved for use in the United States (U.S), but calls to U.S. Poison Centers of exposures began occurring in the late 2000's and substantially increased throughout the 2010's. Phenibut has been deceptively marketed in Virginia as both an antianxiety and a nootropic substance (a substance that improves cognitive abilities). However, the Food and Drug Administration (FDA) has stated that it does not meet the definition of a supplement and has sent warning letters to multiple companies selling phenibut. Phenibut has been listed under several other names including "Pgaba" and "phenigamma". It replaced tianeptine in some ZaZa Red products.

How does Phenibut Work?

Phenibut is a structural analog to GABA that works primarily as a GABA-B receptor agonist with some stimulation of dopaminergic receptors as well. This places phenibut in a similar drug category to common sedatives such as baclofen and gamma-hydroxybutyrate (GHB).

Phenibut also appears to inhibit Beta-phenylethylamine (PEA) release. PEA is an endogenous neuroactive monoamine that is related to anxiety. It is the combination of these effects that has lead phenibut to be marketed as a nootropic medication. Although it is important to note that nootropic does not have a single agreed upon medical definition and is used primarily for individual medication marketing rather than for pharmacologic research.

Symptoms and Management

Phenibut toxicity presents similar to a classic sedative-hypnotic toxidrome with drowsiness and lethargy being the most commonly reported symptoms. A recent review of phenibut cases found that close to half of patients in 36

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published cases required intubation for severe central nervous system (CNS) depression. There appears to be a significant number of patients who develop movement disorders including tremors, dystonia, or myoclonus as well as psychotic symptoms ranging from auditory/visual hallucinations to mania and delusions. Seizures can develop as well due to agonism of GABA-B receptors leading to feedback inhibition of presynaptic GABA-A neurons.
Treatment of phenibut toxicity is primarily supportive and includes airway monitoring and intubation, intravenous fluids, and potentially benzodiazepines for seizures.

Phenibut Withdrawal

Phenibut withdrawal remains a significant area of concern as well. Daily use appears to be correlated with risk of withdrawal symptoms possibly related to phenibut's short half-life and impacts on the GABA and dopaminergic systems. Many patients require doses of the medication multiple times a day to avoid withdrawal.

Withdrawal symptoms most commonly include anxiety, insomnia, and psychotic symptoms such as hallucinations, delusions, and paranoia. Over half of reported patients in a recent literature review also had movement disorders such as tremors, rigidity, myoclonus, or catatonia and withdrawal seizures have been reported.

Treatment of phenibut withdrawal is not well studied and guidelines are still emerging. The most used medications are benzodiazepines and/or baclofen due to similar mechanisms of action. Benzodiazepines have been used less in the outpatient setting due to concern for abuse. However, dosing strategies remain highly variable. No clinical studies have been conducted to guide management strategies.

Recent Trends in Phenibut

Phenibut cases as reported to the National Poison Center Database System had a notable increase through the 2010's from 72 cases in 2015 up to 330 cases by 2019. Cases numbers have remained consistent in recent years with cases ranging between 250 and 325 from 2020 until 2023. Phenibut remains easily accessible for purchase via the internet. Multiple case reports confirmed online storefronts as the source of the patient's phenibut. Commonly cited reasons people purchase phenibut include benzodiazepine replacement and managing withdrawal from

benzodiazepines, opioids, and alcohol.

There are no FDA approved uses for phenibut. Despite warnings from the FDA, multiple brands have continued to freely sell phenibut online. Production of phenibut is not regulated and drug content can vary significantly A recent study has found that the quantity of phenibut in multiple supplements actually increased after the FDA issued warning. Some supplements have had dosages up to 1,164 mg vs the 250 mg that is more commonly prescribed in Russia. As of 2026 phenibut has not been made a scheduled drug by the federal government and no Virginia state laws exist regulating its production, sale, or use.

Summary

Phenibut is a GABA-B agonist that exists as a grey market medication often marketed as a supplement and nootropic despite no being approved by the FDA. It is available online for purchase and reported cases have remained consistent after an initial rise in the late 2010s. Toxicity presents similarly to more traditional GABA agonists such as ethanol and benzodiazepines but with a high propensity for movement disorders. Seizures have been reported possibly due to GABA-A feedback inhibition.

Treatment is primarily supportive care focusing on respiratory monitoring. Withdrawal remains a significant concern due to phenibut's short half-life and management has focused on benzodiazepines and baclofen use. If questions arise, please do not hesitate to contact the UVA Health's Blue Ridge Poison Center 24/7/365 at 1-800-222-1222. You may also reach our center directly using the dedicated health provider hotline: 1-800-451-1428.

References available upon request.