October 30, 2020

Drug Safety Communication: Stronger Warning Labels for Benzodiazepines

Benzodiazepines are used to treat a variety of conditions, including generalized anxiety disorder, insomnia, seizures, social phobia, and panic disorder. They are also used before some medical procedures as a premedication. On September 23, 2020, the U.S. Food and Drug Administration (FDA) announced a requirement that the *Boxed Warning* must be updated for all benzodiazepines to address the serious risks of abuse, misuse, addiction, physical dependence, and withdrawal reactions.

Benzodiazepines are widely prescribed and even when taken at recommended dosages, can lead to misuse, abuse, and addiction. The FDA found the current prescribing information for benzodiazepines does not provide adequate warnings about these serious risks, so they may be prescribed and used inappropriately. These risks increase even more when benzodiazepines are used together with alcohol, prescription opioids, and illicit drugs. Physical dependence can occur when benzodiazepines are taken steadily for several days to weeks, even as prescribed. Stopping the use of benzodiazepines suddenly or reducing the dose too quickly can result in serious withdrawal reactions, including seizures, which can be life-threatening.

Changes will also be required for the Medication Guide, as well as several other sections of the prescribing information, including the *Warnings and Precautions*, *Drug Abuse and Dependence*, and *Patient Counseling Information* sections. According to the FDA, these actions were based on a review of post-marketing databases, reports of adverse event cases, and published literature on hazardous use, misuse, addiction, physical dependence, and withdrawal associated with the use of benzodiazepines.

Health care providers should take the following actions before prescribing benzodiazepines:

- Consider all therapeutic options for management of the patient's condition, and provide information about non-drug alternatives to help with stress, anxiety, insomnia, etc.
- Warn patients and caregivers about the risks of abuse, misuse, addiction, dependence, and withdrawal with benzodiazepines and the associated signs and symptoms. Also alert them of the serious risks of taking benzodiazepines with alcohol or other substances, including opioids.
- Limit both the dosage and duration of benzodiazepine use to the minimum needed to achieve the necessary clinical effect.
- Use caution when a patient is already taking opioids and other central nervous system (CNS) depressants, as this can lead to serious side effects, including severe respiratory depression and death.
- Assess and monitor patients for signs and symptoms of abuse, misuse, or addiction

When it is clinically appropriate for a patient to discontinue benzodiazepines or reduce the dosage, it is important to do so while also reducing the risk of acute withdrawal reactions. Health care providers should use a patient-specific plan to taper the dosage of the benzodiazepine gradually. If a patient is experiencing withdrawal symptoms, it may be necessary to pause the taper for a period of time or increase the benzodiazepine to the previous dosage and then once stable, proceed with a more gradual taper.

To read the full safety announcement, which includes a full list of precautions, refer to the "FDA requiring Boxed Warning updated to improve safe use of benzodiazepine drug class" article found on the Drug Safety and Availability page of the FDA website.