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# The Medical Letter®

### on Drugs and Therapeutics

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#### IN BRIEF

### **New Benzodiazepine Warnings**

The FDA now requires boxed warnings in the package inserts of benzodiazepines describing the potential for these drugs to be abused and misused and to cause addiction and physical dependence.1 Benzodiazepine labels have contained a boxed warning about a risk of serious drug interactions with opioids since 2016.2

Benzodiazepines act by potentiating the effects of the inhibitory neurotransmitter GABA in the CNS. Although their abuse potential is less than that of opioids, they are often misused concurrently with opioids and alcohol, which can markedly increase the risk of overdose and death. Patients with a history of drug or alcohol abuse are more likely to develop a benzodiazepine use disorder. Abrupt withdrawal of benzodiazepines after chronic use can result in serious, potentially life-threatening adverse effects such as seizures. Benzodiazepines are classified by the DEA as schedule IV controlled substances.

Postmarketing data and published literature have shown an increasing rate of benzodiazepine-associated morbidity and mortality over the past decade. In 2016, more emergency department visits in the US were associated with benzodiazepine use than with opioid use (167,845 vs 129,863),3 and in 2018, it was estimated

that 5.4 million Americans ≥12 years old had abused or misused benzodiazepines in the previous 12 months.4 From 2010 to 2017, annual benzodiazepine-associated deaths in the US increased 8.9-fold to 11,537. Most benzodiazepine-related serious adverse effects and emergency department visits involved concurrent use of other drugs.3,5

Benzodiazepines should be used at the lowest effective dose for the shortest possible duration of time, and patients receiving them should be monitored for substance use disorders. The dose should be tapered gradually when stopping chronic treatment. 6

- 1. FDA drug safety communication: FDA requiring Boxed Warning updated to improve safe use of benzodiazepine drug class. September 23, 2020. Available at: https://bit.ly/3nJJzle. Accessed October 22, 2020.
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- 3. Al Geller et al. U.S. emergency department visits resulting from nonmedical use of pharmaceuticals, 2016. Am J Prev Med 2016; 56:639.
- 4. Substance Abuse and Mental Health Services Administration. 2018 NSDUH detailed tables. Available at: https://bit.ly/3khrqPU. Accessed October 22, 2020
- 5. CDC. National Vital Statistics System: mortality statistics. Available at: https://bit.ly/3IZgAhQ. Accessed October 22, 2020.
- 6. M Soyka. Treatment of benzodiazepine dependence. N Engl J Med

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