



## **CONCURRENT USE OF OPIOIDS AND BENZODIAZEPINES**

In August 2016, a U.S. Food and Drug Administration (FDA) review found that the growing combined use of opioid medicines with benzodiazepines or other drugs that depress the central nervous system (CNS) has resulted in serious side effects, including slowed or difficult breathing and deaths. Opioids are used to treat pain and cough; benzodiazepines are used to treat anxiety, insomnia, and seizures. In an effort to decrease the use of opioids and benzodiazepines, or opioids and other CNS depressants, together, the FDA has added Boxed Warnings to the drug labeling of prescription opioid pain and prescription opioid cough medicines, and benzodiazepines.

### **RATIONALE BEHIND WARNING**

The FDA's data review showed physicians have increasingly been prescribing opioids and benzodiazepines together, and this practice has been associated with adverse outcomes.

Specifically, the agency found that from 2004 to 2011, the rate of emergency department visits involving non-medical use of the two drug types together increased significantly, with overdose deaths (from taking prescribed or greater than prescribed doses) involving concomitant use nearly tripling during that period.

Additionally, the number of patients who were prescribed both an opioid analgesic and (a) benzodiazepine increased by 41 percent between 2002 and 2014, which translates to an increase of more than 2.5 million opioid analgesic patients receiving benzodiazepines.

The FDA's actions on this issue are consistent with the CDC's [guideline for prescribing opioids for chronic pain](http://www.cdc.gov), ([www.cdc.gov](http://www.cdc.gov)) which includes warnings about the potential harms of co-prescribing opioids and benzodiazepines.

### **WHAT THIS MEANS FOR PHYSICIANS**

- increasing numbers of patients are being prescribed both classes of medications;
- increasing numbers of patients are sustaining fatal and nonfatal overdoses attributable to the combination of medications;
- the two classes of medications depress respiratory drive via different chemical pathways and can, therefore, demonstrate an additive effect in suppressing respiration; and
- patients taking a combination of the two classes of drugs are at higher risk for overdose compared with patients taking just one or the other.

Physicians should carefully assess each patient who takes both classes of medications regarding the need to continue to take both drugs, with the goal of tapering and/or discontinuing one or the other class of medications.

If the physician, after discussing the pros and cons of the medication classes with the patient, feels that both classes of medications should be continued (with the patient's consent), he or she should prescribe the lowest effective dose to achieve functional improvement.

In addition, for patients taking both classes of medications, physicians should consider using a non-sedating antidepressant or related medication in place of the benzodiazepine, because these patients may actually have untreated depression or a related disorder that is being masked by the use of benzodiazepines. Physicians should also be aware of the possible additive effect of using codeine-containing cough preparations in patients who are taking both classes of medications.

### **SUMMARY**

Health care professionals should limit prescribing opioid pain medicines with benzodiazepines or other CNS depressants only to patients for whom alternative treatment options are inadequate. If these medicines are prescribed together, limit the dosages and duration of each drug to the minimum possible while achieving the desired clinical effect. Warn patients and caregivers about the risks of slowed or difficult breathing and/or sedation, and the associated signs and symptoms. Avoid prescribing prescription opioid cough medicines for patients taking benzodiazepines or other CNS depressants, including alcohol.

### **FACTS ABOUT OPIOIDS AND BENZODIAZEPINES**

- Opioids are powerful prescription medicines that can help manage pain when other treatments and medicines cannot be taken or are not able to provide enough pain relief. Opioids such as codeine and hydrocodone are also available in combination with other medicines to treat coughing.
- Common side effects of opioids include drowsiness, dizziness, nausea, vomiting, constipation, and slowed or difficult breathing. Opioids also carry serious risks, including misuse and abuse, addiction, overdose, and death.
- Benzodiazepines are a class of medicines that are widely used to treat conditions including anxiety, insomnia, and seizures.
- Common side effects of benzodiazepines include drowsiness, dizziness, weakness, and physical dependence.
- Both opioids and benzodiazepines depress the central nervous system (CNS).
- Both opioids and benzodiazepines are commonly prescribed drugs. In 2014 in the U.S., 81 million patients were dispensed an opioid, and 30 million patients were dispensed a benzodiazepine.

## **ADDITIONAL INFORMATION FOR HEALTH CARE PROFESSIONALS**

- Concomitant use of opioid pain or cough medicines and benzodiazepines, other central nervous system (CNS) depressants, or alcohol may result in profound sedation, respiratory depression, coma, and/or death.
- Reserve concomitant prescribing of opioid analgesics with benzodiazepines or other CNS depressants for use in patients for whom alternative treatment options are inadequate.
- Avoid use of prescription opioid cough medications in patients on benzodiazepines or other CNS depressants.
- If the decision is made to concomitantly prescribe a benzodiazepine or other CNS depressant for an indication other than epilepsy with an opioid analgesic, prescribe a lower initial dose of the benzodiazepine or other CNS depressant than indicated in the absence of an opioid, and titrate based on clinical response.
- If an opioid analgesic is initiated in a patient already taking a benzodiazepine or other CNS depressant, prescribe a lower initial dose of the opioid, and titrate based on clinical response.
- Monitor patients closely for respiratory depression and sedation.
- Advise both patients and caregivers about the risks of respiratory depression and sedation if opioids are used with benzodiazepines, alcohol, or other CNS depressants (including illicit or recreational drugs).
- Advise patients not to drive or operate heavy machinery until the effects of concomitant use of the opioid and benzodiazepine or other CNS depressant have been determined.
- Screen patients for risk of substance-use disorders, including opioid abuse and misuse, and warn them of the risk for overdose and death associated with the use of additional CNS depressants, including alcohol and illicit or recreational drugs.
- Encourage patients to read the Medication Guides or patient information leaflets that come with their filled prescription(s).

### References:

FDA Drug Safety Communication: FDA warns about serious risks and death when combining opioid pain or cough medicines with benzodiazepines; requires its strongest warning. <https://www.fda.gov/drugs/drug-safety-and-availability/fda-drug-safety-communication-fda-warns-about-serious-risks-and-death-when-combining-opioid-pain-or>. Accessed December 2020.

FDA Requires New Warnings on Combined Opioid, Benzodiazepine Use. <https://www.aafp.org/news/health-of-the-public/20160907opioid-benzos.html>. Accessed December 2020.