

Opioids and Benzodiazepines – Safety Communication

- On August 31, 2016, the [FDA announced](#) that *Boxed Warnings* will be added to the drug labels for opioids, prescription opioid cough medicines, and benzodiazepines (BZDs), stating that the combined use of these products or other drugs that depress the central nervous system (CNS) has resulted in serious side effects, including slowed or difficult breathing and deaths.
 - Related revisions will be made to the *Warnings and Precautions*, *Drug Interactions*, and *Patient Counseling Information* sections of the labeling. Medication Guides will also be updated.
- Opioids are used to treat pain severe enough to warrant use of an opioid when other pain medicines cannot be taken or are not able to provide enough pain relief. They also have serious risks including misuse, abuse, addiction, overdose, and death.
 - Opioids such as codeine and hydrocodone are also approved in combination with other medicines to reduce coughing [eg, [promethazine with codeine](#) and [Tussionex® Pennkinetic® \(hydrocodone polistirex/chlorpheniramine polistirex\)](#)].
- BZDs are used to treat anxiety, insomnia, and seizures.
- Health care professionals should limit prescribing opioid analgesics with BZDs or other CNS depressants only to patients for whom alternative treatment options are inadequate.
 - If these medicines are prescribed together, the dosages and duration of each drug should be limited to the minimum possible while achieving the desired clinical effect.
 - Patients and caregivers should be warned about the risks of slowed or difficult breathing and/or sedation, and the associated signs and symptoms.
 - Patients should be screened for risk of substance-use disorders prior to opioid therapy.
 - Prescribing opioid cough medicines should be avoided for patients taking BZDs or other CNS depressants, including alcohol.
- Patients taking opioids with BZDs, other CNS depressant medicines, or alcohol; and caregivers of these patients should seek medical attention immediately if they or someone they are caring for experiences symptoms of unusual dizziness or lightheadedness, extreme sleepiness, slowed or difficult breathing, or unresponsiveness.
 - Patients should not drive or operate heavy machinery until the effects of concomitant use of the opioid and BZD or other CNS depressant have been determined.
 - Patients should direct any questions they may have regarding opioids, BZD or other medicines with their healthcare provider.
- The safety update is based on a review of studies that showed an increasing trend in concomitant dispensing of opioids and BZDs, and an increasing frequency of combined BZD and prescription opioid misuse, abuse, and overdose, as measured by national emergency department visit and overdose death rates.

- Recent studies in the literature show that concomitant use of opioids and CNS depressants other than BZDs, including alcohol, is also associated with serious adverse events.
 - One study analyzed the involvement of other CNS depressants (eg, barbiturates, antipsychotic and neuroleptic drugs, antiepileptic and antiparkinsonian drugs, anesthetics, autonomic nervous system drugs, and muscle relaxants) and death and found that these drugs were contributing factors in many cases where opioid analgesics were also implicated.
 - The reviewed studies are based on opioids; however, due to similar pharmacologic properties, there would be similar risks with concomitant use of opioid cough medications and BZDs, other CNS depressants, or alcohol.
- Due to the unique medical needs and benefit/risk considerations for patients taking medication-assisted therapy (MAT) (eg, [buprenorphine](#)), the FDA is continuing to examine data regarding concomitant use of BZDs and MAT.
- The FDA is evaluating whether labeling changes are needed for other CNS depressants, and will update the public when more information is available.



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