Practical Considerations for Prescribing Benzodiazepines and Opioids

JAMES. V. McDONALD, MD, MPH; VICTORIA AYERS, ASCJ; JACKIE PAQUIN

INTRODUCTION

The Food and Drug Administration is responsible for evaluating and approving the medications we prescribe. The FDA reviews post-market experience and monitors adverse drug reactions or unexpected effects. One of the strictest warnings the FDA can apply to a medication is a Boxed warning or Black Box warning. *"Drugs that have special problems, particularly ones that may lead to death or serious injury, may have this warning information displayed within a box in the prescribing information. This is often referred to as a "boxed" or "black box" warning. Drugs that have such boxed warnings are not permitted to have reminder ads."*[1]

In August of 2016, the FDA issued a Black Box warning regarding co-prescribing of benzodiazepines2 and opioids:

Important Information for Patients

FDA is warning patients and their caregivers about the serious risks of taking opioids along with benzodiazepines or other central nervous system (CNS) depressant medicines, including alcohol. Serious risks include unusual dizziness or lightheadedness, extreme sleepiness, slowed or difficult breathing, coma, and death. These risks result because both opioids and benzodiazepines impact the CNS, which controls most of the functions of the brain and body.

- *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. They are also approved in combination with other medicines to reduce coughing. Common side effects include drowsiness, dizziness, nausea, vomiting, constipation, and slowed or difficult breathing. Opioids also carry serious risks, including misuse and abuse, addiction, overdose, and death. Examples of opioids include oxycodone, hydrocodone, codeine, and morphine.*
- *Benzodiazepines are drugs prescribed to treat conditions like anxiety, insomnia, and seizures. Examples of these drugs include: alprazolam, clonazepam, and lorazepam. Common side effects include drowsiness, dizziness, weakness, and physical dependence.*

If you are taking both opioids and benzodiazepines together, consult your health care provider to see if continued combined use is needed. For more information, please see the ***FDA Drug Safety Communication."***[3]

This black box warning requires the prescriber to thoughtfully consider the warning and interpret the concomitant risks and benefits. It is important to discuss these risks and benefits with the patient when establishing a treatment plan.

DATA ON CO-PRESCRIBING OF BENZODIAZEPINES AND OPIOIDS

Figure 1 illustrates annual doses of benzodiazepines, opioids and respective combinations of benzodiazepines and opioids. In 2015, there were over 17 million doses of benzodiazepines prescribed to patients already taking an opioid; in 2016, this rose to almost 22 million doses. Conversely, in 2015, almost 21 million doses of opioids were given to patients who were taking a benzodiazepine; in 2016, this number increased to almost 26 million doses.

Figure 1.

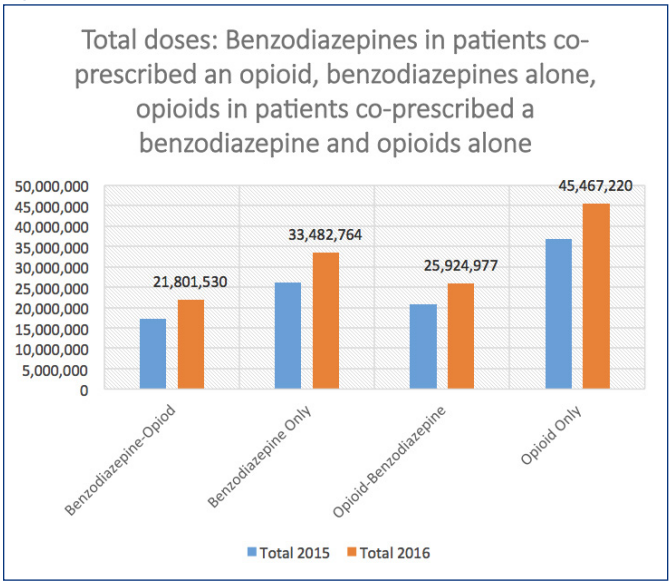

Figure 2 illustrates are active licensees by discipline for physicians, advanced practice registered nurses, dentists and physician assistants, followed by the number of that group who have at least one patient in 2016 who was prescribed a benzodiazepine and an opioid in the same 30-day period. It is evident that about 50% of all prescribers have at least one patient who has been prescribed a benzodiazepine and an opioid in 2016.

Figure 2.

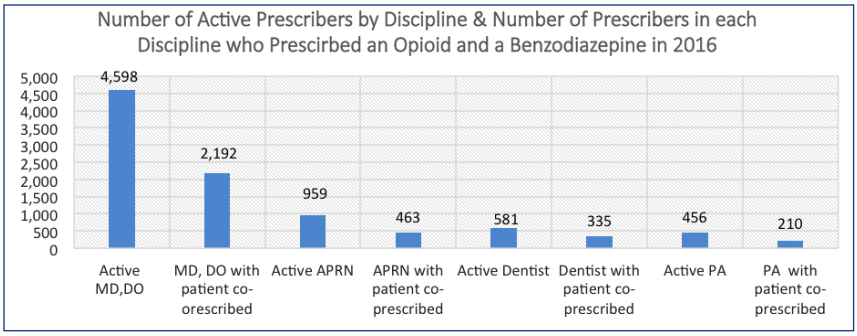

Figure 3.

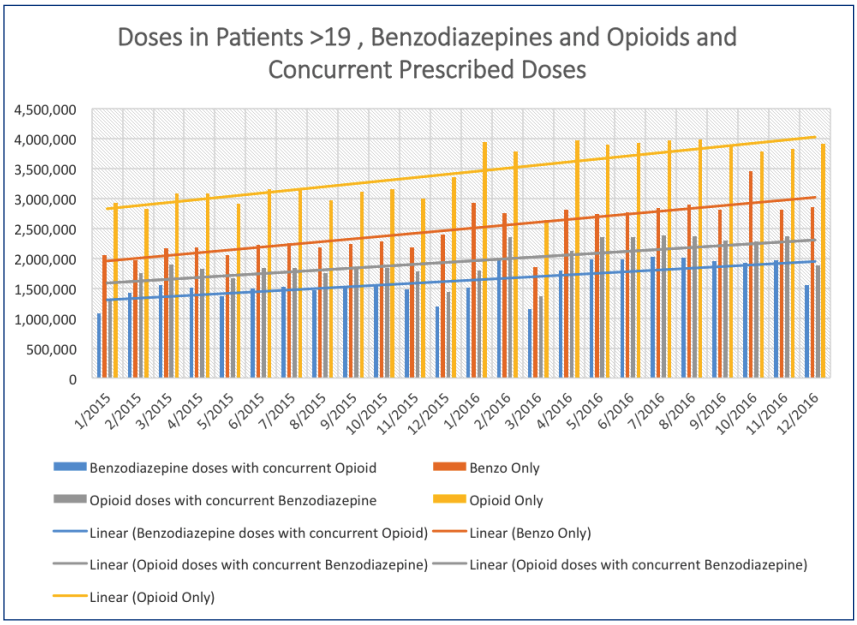

Figure 3 illustrates monthly prescribed doses of benzodiazepines and opioids over a two year period from January 2015 to December 2016. These data demonstrate an increasing trend in the prescribing of benzodiazepines, opioids and combinations of benzodiazepines and opioids.

RECOMMENDATIONS WHEN PRESCRIBING A BENZODIAZEPINE FOR A PATIENT ALREADY TAKING AN OPIOID

Prescribers should be very thoughtful when prescribing any controlled substance. The nature of the black box warning regarding benzodiazepines and opioids require prescribers to educate patients and prescribe judiciously.

There are three overarching concepts regarding co-prescribing benzodiazepines and opioids that prescribers should strongly consider.

Overarching Concepts

1. Stop Starting
2. Taper, titrate and do not escalate
3. Monitor closely

Stop Starting: Prescribers have a duty to warn patients about the potential for adverse outcomes due to the combination of a benzodiazepine and an opioid. Prescribers should additionally warn patients about the added risk when patients co-ingest alcohol. The black box warning specifically requires education regarding potential adverse events: "*unusual dizziness or lightheadedness, extreme sleepiness, slowed or difficult breathing, coma, and death.*"

Prescribers are already required when prescribing an opioid to educate patients.[4] If prescribers must start a benzodiazepine, this should be done with a short course planned (no more than 2–4 weeks). There should be a clear expectation regarding anticipated clinical benefit and a plan for stopping if side effects.

Taper, titrate and do not escalate: Patients who are already on a benzodiazepine and an opioid are at increased risk.[5] Prescribers should review with the patient the risks and benefits of the current therapy and decide if tapering of either or both medications is appropriate. Consideration should be given to a functional assessment of each patient and optimizing functional outcome based on treatment goals. Achieving a pain free status may not be possible. A thoughtful consideration of alternatives to medication should be considered as well.

Tapering benzodiazepines can be done via several different methods and there are resources available for review to consider.[6,7,8,9,10] There are also several resources for tapering opioids that prescribers may find useful.[11,12] The CDC pocket guide is one such resource. Deciding whether to taper the benzodiazepine or opioid first is a decision that may be made with the patient, considering risks, benefits and treatment goals.

If medications cannot be tapered, the dose(s) should be carefully titrated to the minimum effective dose. Consideration needs to be given to the ability to function and to perform activities of daily living.

Tolerance is an issue with each of these medications. Prescribers are reminded not to escalate a patient's dose without a clear treatment goal. Patients should be carefully evaluated prior to dose increases and risks and benefits reviewed.

Monitor Closely: Existing regulations detail minimum requirement for patients on opioids.[13] Patients who are also prescribed a benzodiazepine are at higher risk. Prescribers must monitor the patient at appropriate intervals. The frequency of visits needs to be customized to the patient and their comorbidities. Patients with coexisting diseases and past history need to be seen more frequently.

SUMMARY

- The FDA has issued a black box warning regarding the combination of benzodiazepines and opioids
- Patients who take benzodiazepines and opioids can experience tolerance, dependence and addiction
- Patients who are co-prescribed benzodiazepines and opioids are at higher risk of overdose
- Prescribers have a duty to warn patients about the risk of these medications
- Stop Starting new patients on the combination of benzodiazepines and opioids
- Taper, titrate and do not escalate dosages of benzodiazepines and opioids in patients being co-prescribed these medications
- Monitor closely all patients on long term (>4 weeks) patients on opioids and benzodiazepines

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Authors

James. V. McDonald, MD, MPH, Chief Administrative Officer, Board of Medical Licensure and Discipline, Rhode Island Department of Health (RIDOH).

Victoria Ayers, ASCJ, Prescription Drug Monitoring Program Data Analytics, RIDOH.

Jackie Paquin, Chief Implementation Aide, RIDOH .