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Reduce Risk of Opioid Overdose Deaths by Avoiding and Reducing Co-Prescribing Benzodiazepines

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PROVIDER TYPES AFFECTED

This MLN Matters article is for physicians, non-physician practitioners (NPPs), other prescribers, and pharmacists who prescribe or dispense opioids and benzodiazepines (BZDs).

PROVIDER ACTION NEEDED

When you prescribe opioids and BZDs to the same patient, there are potential negative consequences, such as:

- Higher risk of overdose deaths[1]
- Higher risk of suicide[2]
- Worse treatment outcomes[3]
- Increased health service use[4]

These are significant risks regardless of whether you prescribe these medications for comorbid chronic pain, anxiety, or insomnia, or if your patients use illicit opioids (for example, fentanyl or heroin) or get BZDs through a non-prescription source.[1] In 2017, 10,010 people died from overdosing with both BZDs and an opioid, which is more than a fifth of the 47,600 total opioid overdose deaths in that year.[5]

This MLN Matters article describes the latest key issues related to co-prescribing BZDs with opioids. It summarizes multiple strategies to reduce the impact of this potentially dangerous practice, with a focus on patient health, safety, and well-being.

Practices to Reduce Co-Prescribing BZDs and Opioids

Consider possible fatal overdoses when weighing the risks and benefits of co-prescribing BZDs and opioids. Most prescribers already use caution when prescribing controlled substances, and the nature of the black box warning for BZDs and opioids requires you to educate patients about the potential risks.[6]

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There are five central principles for co-prescribing BZDs and opioids:

1. ***Avoid initial combination by offering alternative approaches***
2. ***If new prescriptions are needed, limit the dose and duration***
3. ***Taper long-standing medications gradually and, whenever possible, discontinue***
4. ***Continue long-term co-prescribing only when necessary and monitor closely***
5. ***Provide rescue medication (for example, naloxone) to high-risk patients and their caregivers***

Carefully discuss the risks and benefits with your patients, including legal representatives if needed, before making changes to medication regimens. This can be challenging as often patients want to continue medications that they feel help them stay stable. You are more likely to succeed when you take an individualized, person-centered approach, and create treatment plans that involve your patients' support networks, including friends, family, and caregivers.[7]

1. Avoid initial combination by offering alternative approaches

Do not start BZDs as an adjunct treatment with opioids for chronic pain due to the lack of evidence and efficacy.[8] Avoid prescribing BZDs along with medication-assisted treatment (MAT) for opioid use disorder (OUD).[9] Even short-term BZD use, on an as needed basis, in patients with long-term opioid use, can be a problem. You should also screen people taking BZDs and prescription opioids for mental disorders, given the frequent comorbidity. Providers must carefully weigh the benefits and risk of each individual's circumstances when making prescribing decisions.

Use caution before co-prescribing BZDs and opioids and make every effort to choose a different treatment plan. For example, use a prescription drug monitoring program (PDMP)--an electronic database that tracks controlled substance prescriptions in a state--as part of the decision-making process to help stratify risk.[10] Proactively communicate with your patients' other health care providers if you are concerned that your patients are getting prescriptions from multiple sources or are using illegal drugs. The Table below lists some alternatives to BZDs and prescription opioids; tailor treatment to each individual's clinical status and other factors.

Table. Alternatives to Benzodiazepines and Opioids

Alternatives to Benzodiazepines	Alternatives to Opioids
• Psychotherapies (for example, cognitive behavioral therapy for anxiety and sleep disorders) • Progressive relaxation techniques • Sleep hygiene • Other medication classes (for example, selective serotonin reuptake inhibitors, tricyclic antidepressants, and buspirone)	• Other medication classes (for example, over the counter and non-scheduled analgesics, serotonin-norepinephrine reuptake inhibitors, and gabapentin) • Psychotherapies (for example, cognitive behavioral therapy, mindfulness, and meditation) • Other treatments (for example, topical medications, trigger point injections, and transcutaneous electrical nerve stimulation) • Complementary and integrative care (for example, acupuncture, physical therapy, exercise, and aquatic therapy)

Where possible, consider prescribing alternative treatments described in the Table, noting that not all treatments are available to or appropriate for all patients.

2. If new prescriptions are needed, limit the dose and duration

If you determine the benefits of co-prescribing BZDs and opioids outweigh the risks, prescribe short-term treatments (such as, 7 or fewer days' supply and no more than 2 weeks). While prescribing medications, tell your patients about the possible adverse outcomes from combining a BZD and an opioid. Warn your patients about the additional risk when patients also drink alcohol or use other substances. Educate your patients about the black box warning for potential adverse events, including "unusual dizziness or lightheadedness, extreme sleepiness, slowed or difficult breathing, coma, and death."[6] If you prescribe BZDs and opioids, you should have a clear expectation regarding the clinical benefit and a plan for tapering the medications when appropriate.

3. Taper long-standing medications gradually and, when possible, discontinue

Your patients who are already on a BZD and an opioid are at increased risk of significant negative outcomes. According to some estimates, eliminating concurrent use of BZDs and opioids could reduce the risk of an emergency department visit or inpatient admission for opioid overdose by as much as 15 percent.[11]

Review, with your patients, the risks and benefits of the current therapy and decide if tapering down either, or both, medications is appropriate based on your patient's unique circumstances.[12] Encourage patient buy-in with a person-centered approach such as motivational interviewing techniques, when possible. Consider functional assessments for your patients to optimize outcomes based on treatment goals. Consider alternatives to controlled medication outlined in the Table above.

Monitor for evidence of misuse or abuse, such as adjusting dosage or frequency in ways other than prescribed or taking medication for indications other than the intended use. For example, patients may take opioids or BZDs for their mood-altering effects. If you suspect misuse or abuse, reemphasize the treatment plan, discuss your concerns with your patient, and consider reducing one or both prescriptions through careful tapering.

You can taper your patient's BZD in several different ways. It can take months or even years to complete a taper. One approach, shown to be effective in a primary care setting, is to convert the BZD to the dose equivalent of a longer-acting BZD then reduce the total dose by 10-25 percent every 1-2 weeks, with close monitoring.[12] This may be too rapid a schedule for some patients to tolerate after using BZDs long-term. Symptom relapse may require smaller dose decreases and longer time intervals between changes. Do not immediately discontinue BZDs as it may:

- Precipitate severe withdrawal, including seizures
- Disrupt sleep
- Increase suicidal thoughts

There are multiple resources to help with tapering BZDs, including:

- VA National Center for PTSD, Effective Treatment for PTSD: Helping Patients Taper from Benzodiazepines
    - https://www.pbm.va.gov/PBM/AcademicDetailingService/Documents/Academic_Detailing_Educational_Material_Catalog/59_PTSD_NCPTSD_Provider_Helping_Patients_Taper_BZD.pdf

You and your patient may also consider working together to taper an opioid; any reduction in opioid dose is always more successful if it is consensual. You may find these resources helpful:

- The Centers for Disease Control and Prevention (CDC) Guideline for Prescribing Opioids for Chronic Pain — United States, 2016 (for adults in primary care settings excluding cancer, palliative care, and hospice)
    - https://www.cdc.gov/drugoverdose/prescribing/guideline.html

4. Continue long-term co-prescribing only when necessary and monitor closely

If your patient has been stable and functional for a long period on both a BZD and an opioid at low or as needed doses, and there is no evidence of problematic use, then decide whether to taper based on the patient's needs and goals, accepting the long-term risks. Discussing possible tolerance should be a foundation of education about the risks and benefits of both medications over time. Even low dose and as needed dosing can be risky.[13] If your patient needs moderate to high doses of either or both medications, you should attempt to taper the dose slowly or document why you are not tapering the dose. Again, consider the approaches in the above Table to help patients concurrently using opioids and BZDs.

You may also consider "contingency prescribing practices" to maintain safety and efficacy as agreed upon with your patients, including safely discontinuing a medication if your patients do not

appropriately follow the prescribed regimen.[14] Adherence monitoring may increase compliance rates and reduce rates of drug misuse among people with chronic pain.[15] This agreement with the patient may include:

- ✓ Getting informed consent for treatment, including risks and benefits
- ✓ Limiting controlled substance prescribing to only one doctor or clinician and getting prescription opioids and BZDs from one pharmacy
- ✓ Giving notice to the patient that the prescriber will get the record of controlled substance prescriptions through the state PDMP
- ✓ Counseling the patient not to use illicit substances or alcohol because of potential interactions

You should employ strategies to empower patients to actively participate in their treatment and maintain responsibility for their appropriate use of prescribed BZDs and opioids. Evaluate patients who are taking opioids in person at least every 3 to 6 months. Patients who chronically use a BZD are at higher risk and may require monitoring more often, depending on their individual risk factors and comorbidities. For high-risk patients, you should complete a baseline urine test. Use point of care urine testing with lab confirmation at your discretion, including breath alcohol tests if indicated. Be aware that many tests do not screen for or often do not detect:

- Alcohol
- Certain BZDs (for example, alprazolam, clonazepam and lorazepam)
- Recently ingested medications
- Low levels of illicit drugs (for example, cannabis and cocaine)[16]

Familiarize yourselves with sensitivities in urine or saliva samples. Consider sending samples to outside laboratories for confirmation, particularly when the result of the drug test is different from that suggested by the medical history, clinical presentation, or self-report.[17]

5. Provide rescue medication (for example, naloxone) to high-risk patients and their caregivers

Given the high risk associated with taking both a BZD and an opioid, you may want to consider a naloxone prescription as a rescue medication for unintentional respiratory suppression. If it is appropriate, discuss naloxone with your patients and their family or caregiver to ensure they know the signs of overdose and how to administer naloxone. When clinically appropriate, prescribers and pharmacists can encourage patients to request naloxone when they fill an opioid prescription. Many states permit pharmacists to dispense naloxone over-the-counter without a prescription.

SUMMARY

Concurrent use of opioids and BZDs presents multiple potential risks and challenges for prescribers and people with chronic pain. You must carefully consider how to approach co-prescribing these medication classes. When possible, take the following steps:

1. Avoid initial combination by offering alternative approaches
   - ✓ Always consider alternatives to opioids for chronic pain
   - ✓ Always consider alternatives to BZDs for anxiety or insomnia
   - ✓ Remember BZDs are not indicated to treat pain
   - ✓ Avoid prescribing BZDs for patients on MATs
   - ✓ Avoid prescribing opioids for patients taking long-term BZDs

2. If new prescriptions are needed, limit the dose and duration

3. Taper long-standing medications gradually and, whenever possible, discontinue
   - ✓ Do not abruptly stop BZDs or opioids
   - ✓ Taper slowly according to guidelines and adjust depending on symptoms
   - ✓ Always work collaboratively with your patients to taper or discontinue

4. Continue long-term co-prescribing BZDs and opioids only when necessary and monitor closely
   - ✓ Clearly explain risks and black box warnings
   - ✓ Closely monitor and consider drug testing at baseline and regularly, especially for high-risk patients
   - ✓ Set clear expectations for what steps will be taken if your patients do not follow the prescribed regimen, including safely discontinuing a medication
   - ✓ Monitor PDMP regularly

5. Provide rescue medication (for example, naloxone) to high-risk patients and their caregivers

ADDITIONAL INFORMATION

- Treatment Improvement Protocol (TIP) 63: *Medications for Opioid Use Disorders* (SMA 18-5063) https://store.samhsa.gov/product/TIP-63-Medications-for-Opioid-Use-Disorder-Pharmacotherapy-for-Opioid-Use-Disorder-Part-3-of-5-/SMA18-5063PT3

- Opioid Overdose Prevention Toolkit (SMA 18-4742) https://store.samhsa.gov/system/files/sma18-4742.pdf

- Federal Guidelines for Opioid Treatment Programs (SMA PEP15-FEDGUIDEOTP) https://store.samhsa.gov/product/Federal-Guidelines-for-Opioid-Treatment-Programs/PEP15-FEDGUIDEOTP

- CDC Guideline for Prescribing Opioids for Chronic Pain—United States, 2016 https://www.cdc.gov/drugoverdose/prescribing/guideline.html

- FDA Drug Safety Communication urging caution about withholding OUD medications from people taking BZDs and concurrent prescribing: “The opioid addiction medications

buprenorphine and methadone should not be withheld from people taking BZDs or other drugs that depress the central nervous system (CNS). The combined use of these drugs increases the risk of serious side effects; however, the harm caused by untreated opioid addiction can outweigh these risks."

- National Center for Complementary and Integrative Health: https://nccih.nih.gov/

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