San Mateo County Health and BHRS Guidelines for the Use of Benzodiazepines (BZDs) and Z-Drugs

PURPOSE: To present updated practice standards that minimize practice variation, maximize evidence-based treatment, improve patient safety and increase patient and provider satisfaction.

BACKGROUND: BZDs are lipid-soluble, gamma-aminobutyric acid (GABA) receptor agonists that quickly cross the blood-brain barrier producing CNS depression and have hypnotic, anxiolytic, muscle relaxant, anticonvulsant, and amnestic properties. Short-acting BZDs (half-life <12hrs) include midazolam, triazolam. Intermediate-acting (half-life 12-24hrs) include alprazolam, lorazepam, and temazepam. Long-acting (half-life >24hrs) include diazepam, clonazepam, clorazepate, chlordiazepoxide, and flurazepam.

BZDs have been associated with increased falls, accidents, cognitive decline, aggressive behaviors, suicide risk, overdose mortality, hazard of death, premature birth and low birth weight, harmful psychological and physical dependence, misuse, and withdrawal. Despite the known risks, BZDs and Z-drugs (zaleplon, zolpidem, eszopiclone) are overprescribed, often as part of treatment plans that are supported by neither scientific evidence nor published guidelines. In 2017 the DEA reports 45.0 million alprazolam, 26.4 million lorazepam, 29.2 clonazepam, 12.6 million diazepam, and 7.0 million temazepam prescriptions in the US. Between 1996 and 2013 the number of adults filling BZD prescriptions increased 67% from 8.1 million to 13.5 million and the percent of adults filling BZD prescriptions increased from 4.1% to 5.6% (2.5%). BZDs are involved in approximately 1/3 of overdose deaths in the US.

In a 2020 study of a Community Mental Health Setting, 19.9% of patients were prescribed at least one BZD. Of those 35.1% had an SUD diagnosis. Of those with an SUD Diagnosis, the odds of receiving a prescription was significantly increased for older patients (age 55 and older), non-Hispanic whites, and women. A study by Agarwal et al published in 2019 found that PCPs accounted for 52.3% of visits involving BZDs in 2015. They also found that BZDs were co-prescribed in 19.2% of visits in which there was also an opioid and that women, middle-aged adults age 45-64 years, whites, those with public insurance were significantly more likely to be prescribed BZDs.

INDICATIONS:

Short-Term (2-4 weeks) Use:

- Urgent treatment of acute agitation, psychosis, or mania. Treatment of Catatonia.
- Urgent medical treatment. Sedation for office procedures or imaging.
- Seizures, spasticity, and a limited number of neurologic disorders.
- Management of alcohol and BZD withdrawal.
- Insomnia (Only if not contraindicated and non-pharmacological and non-controlled pharmacological options have been exhausted. Should not exceed 2 weeks. Sleep studies have shown that sleep patterns return to pre-treatment levels after only a few weeks of regular use. Temazepam is the only BZD with an indication for insomnia.)
- Anxiety (only if not contraindicated and only as a bridge to non-controlled medication and non-pharmacological treatment options. Continuing beyond 2 weeks will result in loss of effectiveness, development of tolerance or dependence, potential for withdrawal symptoms, persistent adverse side effects, and interference with the effectiveness of definitive medications and counseling.)

Long-Term (2 months or more) Use: BZDs and Z-drugs are NOT recommended for long-term use except in exceptional circumstances (e.g., terminally ill).

CONTRAINDICATIONS:

- Any active substance use disorder or history of substance use disorder.
- Currently taking any opioid or stimulant (prescribed or unprescribed).

- Currently taking another BZD, Z-Drug, or muscle relaxant (prescribed or unprescribed).
- Medical and mental health problems that may be worsened by BZDs.
- Cardiopulmonary disorders such as asthma, sleep apnea, chronic obstructive pulmonary disease, and congestive heart failure, as benzodiazepines may worsen hypoxia and hypoventilation.
- Cognitive disorders, history of traumatic brain injury, falls.

RELATIVE CONTRAINDICATIONS:

- Age 65 years and over: (2019 BEERS Criteria strong recommendation to avoid)
    - Are especially vulnerable to the adverse effects, as metabolic capacities decline with age.
    - Are more susceptible to CNS depression and cognitive impairment, and may develop confusion states and ataxia, leading to falls and hip fractures.
    - At risk of drug interactions with other medications.
- Pregnancy
- Post-traumatic Stress Disorder (not clinically recommended).

RECOMMENDATIONS:

New Prescriptions:

- Avoid starting new BZD and Z-Drugs whenever possible.
- Z-drugs are not "safer" than BZDs. Patients on BZDs should not be switched to Z-drugs.
- Confirm no contraindications. Confirm that all appropriate non-pharmacologic and non-controlled pharmacologic options have been exhausted. Consult as appropriate for additional alternatives and Wellness Resources.
- For insomnia, provide psychoeducation that Cognitive Behavioral Therapy for Insomnia is more effective than hypnotics with no side effects. The CBT-i Coach guides the patient through a structured program, to be used with their health provider. Provide Sleep Hygiene information, Insomnia Coach App, and handout on Important Facts about Sleep Medications. Consider alternatives (melatonin, trazodone).
- Check CURES.
- Complete Controlled Medication Agreement with patient.
- Always prescribe the lowest dose of BZD for the shortest time possible.
- Advise the patient regarding the anticipated duration of treatment. Use of BZDs beyond 2 weeks is not recommended. Discuss with the patient in advance, so they agree to discontinuation plan.
- Many patients will have difficulty discontinuing. Have a plan in place to discontinue the BZD in your work with the patient.
- Review the potential risks, benefits and alternatives of BZDs, Z-drugs; and document discussion.
- Caution patients about risk of respiratory depression with alcohol, sedatives, and opioids and document education provided. Consider Narcan prescription and training as appropriate.
- If it is necessary to prescribe BZDs to adults older than 65, consider initiating the medication at half the adult dose. Avoid diazepam (case reports it may be associated with delirium). For older adults, BZDs that don't accumulate metabolites are safest (lorazepam, oxazepam, temazepam). Lorazepam is typically best in this population based on available dosing options (0.5, 1, 2 mg tabs, or 2 mg/mL oral solution).

Managing Existing Prescriptions:

- Given the frequency of BZD prescriptions, clinicians may encounter patients who have been prescribed BZDs or Z-Drugs on a long-term basis. Many may be unwilling and/or afraid to discontinue them.
- Provide education on your concerns of chronic BZD or Z drug use in the first meeting.
- Check CURES at least every 4 months.
- Complete Controlled Medication Agreement with patient. Patients to receive all BZD prescriptions from one designated prescriber and one pharmacy (whenever possible).

- That one prescriber should also be responsible for prescribing other medications with abuse potential, specifically central nervous system (CNS) stimulants and narcotics; if not possible, the prescriber of BZDs should closely coordinate with those prescribing other controlled medications.
- Establish regular monitoring visits that occur at a frequency based on the patient's risk.
- Check a Urine Drug Screen: Discuss with the patient before the UDS about the purpose of testing, what will be screened for and how the UDS result will affect the medications they are prescribed.

Discontinuing Existing Prescriptions:

- Any patient taking BZDs or Z-Drugs for longer than a month should be encouraged to discontinue use. Prioritize in the following situations:
  - 65 years or older
  - Taking multiple BZDs, at supratherapeutic doses or combined with opioids.
  - Cognitive disorder or history of traumatic brain injury.
  - Current or prior history of substance use disorder.
  - Patients who are having falls.
- Each patient's taper will need to be tailored to the individual's needs based on acute versus chronic medical or psychiatric conditions. Plan to taper slowly and provide supportive resources as necessary. Create a treatment plan or schedule to help the patient with this process.
- Physiologic dependence will occur for most patients with chronic BZD use. It is important to distinguish physical dependence from addiction.
- Assess the patient's underlying condition for which the drugs were originally prescribed. Discuss alternatives treatments which may include:
  - Psychotherapy (e.g., CBT, acceptance commitment therapy); Relaxation and Wellness.
  - Antidepressant medications (e.g., SSRIs, SNRIs, tricyclic antidepressants, buspirone)
  - Sleep Hygiene, Insomnia Coach, CBT-i Coach, melatonin, trazodone.
- For patients reluctant to stop BZDs, discuss the benefits of tapering to a lower dose. Set the expectation of revisiting the topic at least annually, and more frequently when there are changes in the patient's care plan or based on provider or patient concerns.

Tapering Process:

- BZD tapers should take place over several weeks to months; sometimes it can be up to years (depending on the person's ability to tolerate the taper, dose, underlying diagnosis, etc.).
- The initial taper should be between 10% and 25% of the total daily dose, then individualized based on the patient's response and tolerability. Tapers faster than 25% increase risk of BZD withdrawal.
- If a patient is struggling with the taper, okay to pause, but avoid going backwards. If needed, provide week at time dispensing to support patient with not self-increasing their dose.
- Maintaining a 50% dose for 1-2 months may be warranted before proceeding further with the taper.
- The last 25% of BZD will often require slower, more gradual taper.
- Switching to long-acting benzodiazepine should be considered for individuals who are:
  - Using short- to intermediate-acting benzodiazepines (e.g., alprazolam).
  - Experiencing difficulty or likely to experience difficulty withdrawing directly due to a high degree of physical or psychological dependency.
- Care should be taken not to taper alprazolam too rapidly or to switch to another BZDs too abruptly, as withdrawal seizures are more prone to occur than with other BZDs.

Acute Withdrawal Signs and Symptoms:

- Anxiety-related withdrawal symptoms are common, and include restlessness, agitation, tremors, dizziness, panic attacks, palpitations, shortness of breath, sweating, flushing, shakiness, difficulty swallowing, poor sleep, sensation of choking, and chest pain.
- Other less common acute withdrawal symptoms include seizures, bowel/bladder problems, changes in appetite, tiredness, faintness, poor concentration, tinnitus, and delirium.

Post-Acute Withdrawal Syndrome (PAWS):

- Some withdrawal symptoms can persist and may take months or years to resolve, including anxiety, fatigue, depression, poor memory and cognition, motor symptoms (pain, weakness, muscle twitches, jerks, seizures), depersonalization, psychosis, paranoid delusions, rebound insomnia, and abnormal perception of movement.

Rapid Tapers:

- Start with 25% dose decrease every 2-4 weeks.
- Consider adding an antiepileptic if concerned about serious withdrawal.
- Indications Include:
  - Concurrent use of illicit substances or urine drug screen results consistent with this.
  - Obtaining BZDs from multiple prescribers or other unsanctioned use of BZDs.
  - Recurring emergency department visits.
  - Patient's behavior suggests possible misuse or diversion of medication.
  - Verbally abusive with staff.
  - Injecting oral/topical benzodiazepines.
  - Unsanctioned dose escalation

BZD dose equivalencies and pharmacokinetics

APPENDIX A: TIPS on conversation with patient our concern about chronic BZDs or Z-Drugs:

- Validate the patient's concerns.
- Keep a positive and encouraging attitude with patients to foster a non-judgmental compassionate approach. Instill hope that patients can get off BZD with the goal to improve their quality of life.
- Reassure patients that support will be provided throughout the taper.
- Provide psychoeducation of side effects and risks of BZDs and discuss no evidence of benefit for BZDs taken for more than 2-4 weeks for any psychiatric condition.
- Provide additional resources (e.g. Resources, Peer Support and Groups, Additional Information).
- Educate the patient about the tapering process and symptoms of withdrawal.
- Recommend non-pharmacological therapies such as cognitive-behavioral therapy, motivational interventions, and development of coping skills and sleep hygiene.
- Involve the patient's family and friends for support and encouragement when appropriate.
- Advise that each person's taper will be unique.
- Advise them that the taper will never go backwards to avoid going through withdrawal again.
- Set expectation with patient that with each step down they likely will have some BZD withdrawal that will likely resolve within 1-2 weeks.

Example script on starting discussion about BZD taper:

Explore treatment history of BZD:

I want to understand your history of being on BZDs or Z drugs. I am curious about when you started taking it, what symptoms was the BZD prescribed to treat, and how those symptoms have changed overtime? What treatment (medication and therapies) have you been tried on for X symptom. [Try to non-judgmentally understand their story and history. Then affirm, reflect what you heard].

Ask permission to provide education on physical dependence:

Would it be okay if I share with you some of my concerns regarding long-term use of this medication? [If they say, yes, and then proceed, if no offer to discuss with them at their next appt.] Overtime, people can develop physical tolerance to the BZD (meaning the desired effect needs more medication over time) and physical dependence (meaning the body will have withdrawal symptoms when the BZD is discontinued).

Validate their concerns about not having the BZD and why they rely on them:

For many people, there is a lot of concern about getting off these drugs/medications and understandably because you've been taking it to help _____ symptom(s).

Provide information and discuss treatment options:

My approach is to help people get off BZDs in a safe and personalized manner and you will be involved with the decision making throughout the process. When you were started on this medication it was probably unknown that there are long-term safety concerns, we now know that long-term use can cause harm for many people. I've helped individuals with successful discontinuation of BZDs and they describe having less anxiety and/or insomnia over time and feel a sense of freedom with no longer feeling the need to take it.

Gauge their interest in tapering:

Here is some information on BZDs [review side effects], have you experienced any of these? What are your thoughts about considering lowering or discontinuing your dose so we can keep you safe? I can offer you safer meds for anxiety or sleep that do not cause physical dependence. Would you be interested in starting a safer medication? [Provider can reference healthcare system recommendation for tapering due to long-term effects of chronic BZD use].

Resources and References:

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6. Overdose Death Rates, National Institute on Drug Abuse.
7. Effective Treatment for PTSD: Helping Patients Taper from Benzodiazepines, National Center for PTSD 2015.
8. The Ashton Manual, The Institute of Neuroscience, Newcastle University.
9. Agarwal SD & Landon BE (2019) Patterns in Outpatient Benzodiazepine Prescribing in the United States, JAMA network open, 2(1), 1-11.
10. American Geriatrics Society 2019 Updated AGS Beers Criteria for Potentially Inappropriate Medication Use in Older Adults. Journal of American Geriatrics Society. 00:1-21, 2019.
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12. Jassell et al (2020). Factors Associated with Benzodiazepine Prescribing in Community Health Settings. J Subst Abuse Treat, Feb 109: 56-60.
13. The ASAM Essential of Addiction Medicine Second Addition 2015; Chapter 44 "Management of Sedative-Hypnotic Intoxication and Withdrawal" p 262-266