Wisconsin Drug Utilization Review

DUR NEWSLETTER

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AFFECTED PROGRAMS

BadgerCare Plus, Medicaid, SeniorCare

TO

Advance Practice Nurse Prescribers With Psychiatric Specialty, Nurse Practitioners, Pharmacies, Physician Assistants, Physician Clinics, Physicians, HMOs and Other Managed Care Programs

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BENZODIAZEPINE PRESCRIBING—APPROPRIATE INDICATIONS AND CHALLENGES

Due to increasing concerns about the long-term use of benzodiazepines, the Wisconsin Drug Utilization Review Board is focused on the challenges of benzodiazepine prescribing, particularly among individuals aged 65 years and older.

The purpose of this newsletter is to encourage prescribers to adopt a circumspect approach when prescribing a benzodiazepine in both acute and chronic clinical situations. The following clinical issues are highlighted in this newsletter:

- Guidelines for treating anxiety disorders
- Risk stratification for benzodiazepine use
- Strategies for safely initiating a benzodiazepine
- Challenges and lessons learned in the management of chronic benzodiazepine use

- Aging patients (65 years of age or older) and prescribing benzodiazepine
- Considerations for deprescribing a benzodiazepine

Guidelines

Many professional organizations have produced well-documented, evidence-based guidelines for treating anxiety disorders, including post-traumatic stress disorder, obsessive-compulsive disorder, panic disorder, generalized anxiety disorder, and social anxiety disorder.

Guidelines include indications for and integration of psychotherapy (especially cognitive behavioral therapy) as well as medication treatment options. Many published guidelines emphasize that benzodiazepines, if indicated at all, are seldom appropriate for more than two to four weeks of use to treat an anxiety disorder. Instead, more support exists for initiating evidence-based interventions such as psychotherapy and possibly an antidepressant.

Benzodiazepines may occasionally be used to treat acute and/or chronic trauma, but alpha and beta adrenergic blockers are potentially more effective choices in blocking nightmares and reducing the anxiety of recurring traumatic memories. Use of a benzodiazepine for insomnia is rarely appropriate for more than one month. The continuation of a benzodiazepine post-hospitalization for sleep can lead to chronic use unless the prescriber is extra vigilant.

Explicit indications for a short-term benzodiazepine medication include:

- Treatment for alcohol withdrawal
- Agitated states of psychosis or mania
- Flying phobias
- Seizures
- Office procedures
- Treatment of spasticity

The chronic use of a benzodiazepine is indicated only in exceptional circumstances and should be carefully evaluated with regard to each individual's clinical situation. Contraindications for use of a benzodiazepine include:

- Concurrent use of another benzodiazepine, hypnotic, muscle relaxant, or opioid

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- An active or historical substance use disorder
- Pregnancy
- Cardiopulmonary disorders where benzodiazepines may exacerbate hypoxia

Refer to the extensive list of annotated references regarding benzodiazepine prescribing included at the end of this newsletter.

Risk Stratification

Initiating a Benzodiazepine

When prescribers are faced with the decision to start a benzodiazepine for an acute situation or to manage chronic benzodiazepine use, the Kaiser Health Foundation guidelines suggest patients who meet the following criteria are at highest risk and require more vigilant monitoring:

- Are age 65 years or older
- Are less than 25 years of age, due to greater risk of substance abuse
- Use polypharmacy with a second benzodiazepine, hypnotic, or opioid
- Have a history of substance use or current alcohol or cannabis use
- Have chronic obstructive pulmonary disease (COPD) or respiratory disease
- Have a history of overdose
- Have post-traumatic stress disorder
- Have an elevated risk for falls
- Are unable to follow a benzodiazepine contract/care plan

Considerations for Initiating a Short-Term Benzodiazepine Trial

The Drug Utilization Review Board has received prescribers' concerns regarding:

- The ability to set limits
- Lack of confidence in using benzodiazepines and reference to guidelines
- Prescribing inconsistency within clinics
- Use of controlled substance medication contracts
- The role of the Prescription Drug Monitoring Program

Prescribers who determine that a trial of a benzodiazepine is indicated should emphasize several patient education issues. Patients need to understand that antidepressants (for example, selective serotonin reuptake

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inhibitors and serotonin-norepinephrine reuptake inhibitors) often require four to six weeks for noticeable therapeutic effects, with a possible subsequent dose increase. While waiting for antidepressant medication to take effect, benzodiazepine may be used for a short time in addition to patient participation in psychotherapy.

Since anxiety is seldom a full 16-hours-per-day, seven-days-per-week disorder, prescribing a lesser monthly quantity may encourage the patient to more carefully consider whether a benzodiazepine is absolutely necessary for coverage of all waking hours. For example, prescribing 45 tablets per month twice daily or 75 tablets or fewer for a three-times-per-day schedule can help the patient be more circumspect on their need for the medication. Since a benzodiazepine is not a viable 24-hour, seven-days-per-week solution, this prescribing approach can help shape the expectation for the patient to mobilize non-medication anxiety-management strategies (for example, exercise, music, relaxation techniques).

Several nationally and internationally established guidelines frame appropriate prescribing of benzodiazepines for various clinical presentations. Prescribers should be confident that their practice of prescribing benzodiazepines follows accepted guidelines for prescribing these controlled substances. Some practices may choose to discuss and develop practice-wide contracts for patients prescribed a benzodiazepine that clearly spell out:

- Refill policies.
- Unacceptable substance use.
- Circumstances under which termination of access to benzodiazepine prescriptions may occur.
- The use of drug screens.
- Polypharmacy issues with opiates and stimulants.

Direct discussions and contracts will help providers be consistent and support collegiality within a clinic. Providers may routinely use the Prescription Drug Monitoring Program resource to manage controlled medications and provide patient education. If patients are aware that clinicians can view all prescriptions for controlled medications prescribed in Wisconsin, they may be more likely to understand how diligently

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state regulatory agencies monitor both the practices and behaviors of prescribers and their patients.

Benzodiazepine Prescribing for Patients Aged 65 Years and Older

Patients aged 65 years and older are especially vulnerable to the adverse effects of benzodiazepines due to decreased metabolic capacities, increased frequency of drug interactions, and potential cognitive impairment. These patients are also more susceptible to the sedation effects of benzodiazepines that can increase the risk of depression, confusion, impaired driving, and an unstable gait that could lead to falls and hip fractures. Geriatric literature documents the concerning risks posed by longer-acting benzodiazepines that may last longer than 24 hours and silently build up, leading to greater blood levels and adverse effects. Daily use may also lead to increased blood levels due to slower metabolism with age, compounded by the drug's inherent long half-life.

Given the potential tolerance of benzodiazepine's effects, patients may complain of a decrease in effect, which can lead to the prescriber increasing daily dosages. With aging, patients may develop additional medical conditions that can lead to polypharmacy in an attempt to manage comorbid illnesses.

The provider chronically prescribing a benzodiazepine for a patient approaching the age of 65 must have a strategy for educating the patient on the increasing risks of benzodiazepines with age as well as a deprescribing plan for the patient.

Inheriting a Patient on a Chronic Benzodiazepine: Challenges and Lessons Learned From Conversations With Wisconsin Medicaid Providers

Through many conversations with different Wisconsin Medicaid providers, the Drug Utilization Review Board has gained an increasing appreciation for the difficult task facing a prescriber and patient on a chronic benzodiazepine regimen. Many patients have never been educated on the risks of tolerance and addiction or risks they will encounter with aging. Deprescribing is critical as a patient approaches age 65, or earlier depending on their overall health. Some prescribers are becoming more concerned about prescribing chronic benzodiazepines, perhaps due to the unfortunate reality of benzodiazepine-opiate overdoses and mortality. The

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risks of benzodiazepines with aging are becoming more widely known as well.

Wisconsin primary care providers have frequently voiced concerns that they often feel "cornered" by their patients who enter their practice stating, "The psychiatrist prescribed this for years so who are you to question my use?" Primary care providers are at a disadvantage as they are not the mental health experts, but they are the front line of mental health care and are well situated to set limits and confront potentially unsafe prescribing practices. Inheriting a patient on a chronic benzodiazepine is an extremely difficult situation that requires patience and trust-building to address.

Fortunately, current prescribing guidelines with robust evidence for limiting chronic benzodiazepine use are available for support. Clinicians can set firm expectations and boundaries in refusing to perpetuate inappropriate benzodiazepine regimens, particularly with new or inherited patients. Many Wisconsin Medicaid providers have shared with the Wisconsin Medicaid psychiatric consultants that it is very helpful to discuss these issues and to reinforce with patients that there are standards of care to follow regarding the use of benzodiazepines.

All prescribers, when initiating a benzodiazepine, have a responsibility to set clear parameters on benzodiazepine use. When a provider inherits an over-medicated or possibly addicted patient with a "legacy prescribing disorder," the new prescriber and patient potentially face many conflicts and suffering. This struggle could have been avoided if the previous (legacy) prescriber had taken care to prescribe benzodiazepines responsibly. Wisconsin Medicaid providers have shared their frustrations with Wisconsin Medicaid consulting staff, citing an underlying sense of helplessness when they inherit a legacy prescribing disorder patient. Deprescribing discussions can be a source of major anxiety for patients and may include an extended process of finding alternate medication approaches in partnership with a new provider.

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Considerations for Deprescribing Benzodiazepines

Successful deprescribing depends on a stable and trusting doctor-patient alliance and requires time, patience, resources, and strategies. While there

is no clearly accepted plan for deprescribing, several different approaches may be used, depending upon:

- Willingness and commitment
- Social supports
- Psychological/psychotherapy support
- Fear of or openness to medication changes
- Current psychiatric disorder
- Severe comorbid medical disorder
- Concurrent stimulants or opioids
- History of seizures
- Long- or short-term benzodiazepine use
- Potential availability of an addiction sub-specialist for consultation

The Kaiser Health Foundation guidelines suggests the use of diazepam for deprescribing off of short-acting benzodiazepines. Refer to the References section at the end of this newsletter. The long half-life of diazepam (20–80 hours) allows for a very slow incremental taper with a reduction of the total daily dose of 10 percent per week or more slowly at 10 percent every two to four weeks, depending on the patient's comorbidities. The same guideline also suggests that for patients over the age of 65, tapering with lorazepam in twice-daily dosing is preferable, since diazepam has been associated with delirium in older patients.

The Canadian government has published an educational handout regarding the risks of benzodiazepines for older patients. This publication includes a day-by-day tapering schedule and is included in the references that follow as well.

U.S. Food and Drug Administration Drug Safety Communication Regarding Benzodiazepines

The U.S. Food and Drug Administration recently released a Drug Safety Communication regarding the use and misuse of benzodiazepines, emphasizing the concerns discussed in this newsletter. The Food and Drug Administration is requiring an update to its most prominent safety warning, the Boxed Warning, and requiring class-wide labeling changes for benzodiazepines. Labeling changes include the risks of abuse, misuse, addiction, physical dependence, and withdrawal reactions to help improve their safe use.

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In addition to labeling changes, the Food and Drug Administration is also requiring changes to the following sections of the prescribing information for all benzodiazepine products:

- Warnings and Precautions
- Drug Abuse and Dependence
- Patient Counseling Information

To help educate patients and caregivers about the risks associated with abruptly stopping benzodiazepines, the Food and Drug Administration also requires revisions to the existing patient medication guides for these medications. The reference and link to the drug safety communication are noted below.

REFERENCES

1. American Psychiatric Association (2020). *Clinical Practice Guidelines*. https://www.psychiatry.org/psychiatrists/practice/clinical-practice-guidelines

   All American Psychiatric Association guidelines are available at the Clinical Practice Guidelines webpage. Review options for the use of benzodiazepines by referring to the following links for diagnosis and treatment guidelines for panic disorder and acute stress disorder:

   a. American Psychiatric Association (Based on January 2009 Practice Guideline). *Treating Panic Disorder: A Quick Reference Guide*. http://psychiatryonline.org/pb/assets/raw/sitewide/practice_guidelines/guidelines/panicdisorder-guide.pdf

   b. American Psychiatric Association (Based on November 2004 Practice Guideline). *Treating Patients With Acute Stress Disorder and Posttraumatic Stress Disorder: A Quick Reference Guide*. http://psychiatryonline.org/pb/assets/raw/sitewide/practice_guidelines/guidelines/acutestressdisorderptsd-guide.pdf

2. Kaiser Foundation Health Plan of Washington (January 2019). *Benzodiazepine and Z-Drug Safety Guideline*. https://wa.kaiserpermanente.org/static/pdf/public/guidelines/benzo-zdrug.pdf

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This resource offers thorough managed care guidance on clinical use of benzodiazepines and Z-drugs with a clear, conservative approach to their use.

3. Katzman, M.A.; Bleau, P. et al., and the Canadian Anxiety Guidelines Initiative Group on behalf of the Anxiety Disorders Association of Canada/Association Canadienne des troubles anxieux and McGill University. BMC Psychiatry (2014). *Canadian clinical practice guidelines for the management of anxiety, posttraumatic stress and obsessive-compulsive disorders*, 14, S1. http://www.biomedcentral.com/1471-244X/14/S1/S1

   The Canadian Psychiatric Study Group on Anxiety Disorders produced this resource on alternatives to benzodiazepines for treatment of anxiety and sleep disorders, recommending a cautious approach to use of benzodiazepines for longer than one month.

4. Lembke, A.; Papac, J. et al. New England Journal of Medicine (2018). *Our Other Prescription Drug Problem*, 378, 693–695. https://www.nejm.org/doi/full/10.1056/NEJMp1715050

   This article provides cautionary recognition of the dangers of the increasing use of benzodiazepines that has been overlooked amidst the opiate crisis and is a call for the vigilant use of prescription drug monitoring programs in monitoring benzodiazepine prescriptions.

5. Martin, P. and Tannenbaum, C. BMJ Open (2017). *A realist evaluation of patients' decisions to deprescribe in the EMPOWER trial*, 7 (e015959). https://bmjopen.bmj.com/content/bmjopen/7/4/e015959.full.pdf

   This Canadian study considers the variables leading to success or failure of efforts to deprescribe benzodiazepines in patients using them chronically.

6. National Institute for Health and Care Excellence (July 2019). *Generalised anxiety disorder and panic disorder in adults: management*. https://www.nice.org.uk/guidance/cg113

   This set of guidelines was developed by the Royal College of Psychiatrists with consistent emphasis on the short-term use of benzodiazepines for anxiety disorders and the preferred use of alternative medications as well as psychotherapy. Refer to the

following guidelines for additional information regarding use of benzodiazepines for mental health disorders:

a. National Institute for Health and Care Excellence (November 2005). *Obsessive-compulsive disorder and body dysmorphic disorder: treatment*. https://www.nice.org.uk/guidance/cg31

b. National Institute for Health and Care Excellence (December 2018). *Post-traumatic stress disorder*. https://www.nice.org.uk/guidance/ng116

c. National Institute for Health and Care Excellence (May 2013). *Social anxiety disorder: recognition, assessment and treatment*. https://www.nice.org.uk/guidance/cg159

7. Soyka, M. New England Journal of Medicine (March 2017). *Treatment of Benzodiazepine Dependence*, 376, 1147–1157. http://doi.org/10.1056/NEJMra1611832

   This article provides a thorough review of the appropriate use of benzodiazepines, the recognition of dependence on benzodiazepines, the treatment of withdrawal, the role of psychotherapy, and the prevention of dependence.

8. Tannenbaum, C., and Institut universitaire de gériatrie de Montréal (2014). *You May Be at Risk*. http://www.criugm.qc.ca/fichier/pdf/BENZOeng.pdf

   This pamphlet is distributed widely in Canada to educate patients on the risks of benzodiazepines with aging. The fifth reference above studied the barriers and successes of using this instrument in working with patients to deprescribe benzodiazepines.

9. U.S. Food and Drug Administration (September 2020). *FDA Requiring Labeling Changes for Benzodiazepines*. https://www.fda.gov/news-events/press-announcements/fda-requiring-labeling-changes-benzodiazepines

10. van Dis, E.A.M.; van Veen, S.C. et al. JAMA Psychiatry (2020). *Long-Term Outcomes of Cognitive Behavioral Therapy for Anxiety-Related Disorders, A Systematic Review and Meta-Analysis*, 77(3), 265–273.

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https://jamanetwork.com/journals/jamapsychiatry/article-abstract/2756136

This article provides a thorough review of cognitive behavior theory for anxiety disorder with and without medications.

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The DUR Newsletter is distributed to prescribers and pharmacies and promotes best practices in drug utilization based on accepted clinical guidelines, U.S. Food and Drug Administration Safety communications, and published peer-reviewed studies. The Wisconsin Drug Utilization Review Board publishes the DUR Newsletter on an as-needed basis.

Wisconsin Medicaid, BadgerCare Plus, and SeniorCare are administered by the Division of Medicaid Services within the Wisconsin Department of Health Services.

To provide feedback or suggestions, prescribers can contact the Pharmacy DUR Team at DHSDUR@dhs.wisconsin.gov.