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# The Effects of Long-Term Benzodiazepine Use and Withdrawal in the Elderly

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This knowledge-based activity is targeted for all pharmacists and is acceptable for 1.0 hour (0.1 CEU) of continuing education credit. This course requires completion of the program evaluation and at least a 70 percent grade on the program assessment questions.

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## Objectives

After completion of this program, the reader should be able to:

1. Explain how benzodiazepines differentially affect the elderly population in terms of pharmacokinetics and pharmacodynamics.
2. Discuss specific adverse effects of benzodiazepines in the elderly population and how these adverse effects impact quality of life.
3. Identify patients who are at highest risk of adverse effects with benzodiazepine use.
4. Describe symptoms of and possible treatments for patients experiencing withdrawal from benzodiazepines.
5. Identify ways a pharmacist can improve medication management in the elderly population.

## Abstract

Benzodiazepines remain a commonly prescribed medication in the United States, and the high usage of this drug class is especially a concern in the elderly population for several reasons. First, elderly patients metabolize drugs differently, leading to varying responses. Age-related changes also have a significant impact on the effects of benzodiazepines. Second, elderly patients are more likely to be taking multiple centrally-acting drugs, which can further exacerbate negative effects. In regard to long-term benzodiazepine use, elderly patients experience an increased risk of cognitive impairment, motor vehicle accidents, decline in physical performance, falls and subsequent fractures, and sleep disturbances. Withdrawal is also a significant concern with long-term benzodiazepine treatment, which can lead to rebound symptoms in addition to mood swings, tremor, headache and loss of appetite. A taper of less than six months is recommended when discontinuing benzodiazepines after use longer than the recommended three month duration of treatment. Pharmacists can have a substantial impact in reducing the detrimental effects of long-term use of benzodiazepines by aiding in the tapering process, as well as identifying inappropriate prescribing and use of benzodiazepines in the elderly population. Overall, pharmacists should be knowledgeable on the appropriate use of benzodiazepines, associated side effects

and withdrawal concerns to reduce the negative effects elderly patients may experience with long-term use.

## Key Terms

Accidental Falls; Aged; Benzodiazepines; Cognition; Hypnotics and Sedatives; Pharmacists; Quality of Life

## Introduction

Despite the potentially detrimental effects of benzodiazepine use, benzodiazepines remain a commonly prescribed medication in the United States. In 2012, Ohio prescribers wrote 41.3 prescriptions for benzodiazepine medications per 100 people, ranking Ohio 20th compared to other states.<sup>1</sup> Ohio is slightly above the national rate of 37.6 prescriptions per 100 people. The high usage of benzodiazepines is especially a concern in the elderly population, in part because elderly patients respond to and metabolize drugs differently. Even if a patient has been on a benzodiazepine for many years, it may begin to have different or more severe adverse effects as the patient ages. Elderly patients, generally defined as 65 years of age and older, are also more likely to be taking several medications, which may include other centrally-acting drugs. The combination of these factors leads to an increased risk of cognitive impairment, motor vehicle accidents, decline in physical performance, falls and subsequent fractures, and sleep disturbances in the elderly population.

Benzodiazepines are included on the American Geriatric Society's Beers Criteria, which notes that elderly patients are known to have higher sensitivity to and slower metabolism of long-acting benzodiazepines, increasing the risk of negative effects.<sup>2</sup> Studies have found these effects can also be seen with short-acting formulations.<sup>3</sup> It can be concluded that if detrimental effects are seen with both short-acting and long-acting formulations of benzodiazepines, then these effects can also be observed with the intermediate-acting medications (Table 1).<sup>4</sup> The Beers Criteria recommendation for benzodiazepine use is classified as 'strong,' meaning that the burdens/risks of use outweigh the potential benefits.<sup>2</sup> Although benzodiazepines may still be an appropriate option in some instances, per the Beers Criteria their use is not recommended in the elderly to treat insomnia, agitation or delirium. Discontinuation of this class of drugs has been associated with some improvement in their negative effects, especially those effects relating to cognition; however, there are still lasting implications with long-term use. The withdrawal process and associated symptoms are also significant, owing to the addictive properties and dependency effects of this class of drugs.<sup>5</sup> As pharmacists, it is important to recognize how these drugs may affect elderly patients differently



**Table 1. Commonly Prescribed Benzodiazepines.**

Short-acting*	Intermediate-acting*	Long-acting*
<ul style="list-style-type: none"> <li>• Midazolam (Versed™)</li> <li>• Triazolam (Halcion™)</li> </ul>	<ul style="list-style-type: none"> <li>• Alprazolam (Xanax™)</li> <li>• Conazepam (Klonopin™)</li> <li>• Diazepam (Valium™)</li> <li>• Lorazepam (Ativan™)</li> <li>• Oxazepam (Serax™)</li> <li>• Temazepam (Restoril™)</li> </ul>	<ul style="list-style-type: none"> <li>• Chlordiazepoxide (Librium™)</li> <li>• Flurazepam (Dalmane™)</li> </ul>

\*classification based on half-life of active components<sup>4</sup>

and to manage these medications accordingly. Pharmacists have an essential role in identifying elderly patients being newly prescribed or currently taking long-term benzodiazepines who may be candidates for other treatment options, making alternative medication recommendations to physicians and assisting patients during the withdrawal process.

Typical and appropriate indications for benzodiazepine use in the elderly include anxiety, panic disorder, sleep disorder and adjustment disorder which are similar to the indications for use in the nonelderly population. However, in some instances such as in a patient who is refractory to standard treatment, benzodiazepines may be appropriately used for short-term treatment of insomnia or agitation even though the recommendation from the Beers Criteria is to avoid use for these indications.<sup>2</sup> Central nervous system (CNS) depression is a typical side effect of benzodiazepines for all age groups. Of significance is that within the older population these side effects are observed more frequently and to a greater extent, and some negative outcomes such as falls, fractures and a decrease in physical performance are unique to the elderly demographic. In the elderly population, these side effects can have substantial implications on the patient's quality of life, autonomy and independence. This increased severity of side effects is due primarily to pharmacodynamic, rather than pharmacokinetic, changes in the CNS and brain that occur naturally with aging and lead to a greater sensitivity to benzodiazepines.<sup>6,7</sup> In fact, elderly patients generally require lower doses of benzodiazepines, corresponding to lower blood concentrations to achieve the effect of sedation, highlighting the increased sensitivity displayed in older patients.<sup>8</sup> The pharmacokinetic changes that occur include changes in the elimination and distribution of benzodiazepines in the aging brain; but, more importantly, the pharmacodynamic changes in the CNS make the receptors more sensitive to the drug.<sup>7</sup> The target for benzodiazepines to produce their CNS effects are the gamma-aminobutyric acid-*a* (GABA<sub>A</sub>) receptors, which are ligand-gated chloride channels. The binding of the benzodiazepine causes the channel to open and results in an influx of chloride, which decreases

neuronal firing.<sup>9</sup> The GABA<sub>A</sub> receptor is made up of several subunits, which contributes to why there are a variety of symptoms associated with this drug class in all patient age groups. The increase in severity of side effects in the elderly may be so extreme for benzodiazepines in particular because GABA<sub>A</sub> receptors are widely distributed throughout the CNS in the spinal cord, cortex, cerebellum, and limbic system, and the distribution of the GABA<sub>A</sub> receptors changes with age, altering the excitability of the brain.<sup>6,9</sup> With the high number of receptors and an increased sensitivity with the aging process, many of the effects seen in a younger person will be exaggerated in the elderly such as greater sedation, less coordination of movement and less inhibition.<sup>7</sup> Changes in psychomotor abilities, reaction time, delirium, coordination and attention are also potential effects of benzodiazepine use in the elderly.<sup>10,11</sup>

### Cognitive Impairments

The use of benzodiazepines can negatively impact cognition or exacerbate normal age-related cognitive decline in elderly patients. However, the length of time the patient is taking the medication is a significant predictor of cognitive decline.<sup>12</sup> Associated risks are increased with the long-term use of benzodiazepines even in those patients who used benzodiazepines chronically and have already successfully discontinued therapy. The length of time a patient has been taking benzodiazepines is a significant predictor of cognitive decline and has been shown to have a greater effect on sustained cognitive impairment compared to the dose alone. Evidence supporting the long-term implications on cognition is varied. Not all patients taking therapeutic doses of benzodiazepines long-term will experience these cognitive and memory impairing effects, or the effects they do experience may be minimal.<sup>12,13</sup> However, several studies have found that cognitive impairment does occur with chronic benzodiazepine use.<sup>10</sup> Central nervous system depression and decline in cognition, alertness and decision-making capacity are all recognized side effects of therapy. Notable short-term effects include anterograde amnesia, or difficulty learning new information, a decrease in mental alertness and the capacity to coordinate

fine movements.<sup>13</sup> Long-term users tend to develop some tolerance to the sedative effects (for example, the drowsiness is less severe over time when compared to initiation of therapy), but effects on memory and cognition continue throughout use. Patients taking benzodiazepines chronically may also struggle to process information quickly and sustain attention on a task for an extended amount of time, as well as have difficulty with visuospatial skills. These effects are more detrimental in the elderly population in terms of severity and persistence of symptoms, even after the medication has been discontinued. These negative cognitive effects impact the elderly patient's quality of life, memory and independence.

The negative effects of benzodiazepine use in the elderly may extend beyond the duration of therapy to a greater extent than in the nonelderly population. Cognitive impairment was found to persist for at least six months after discontinuation, in comparison to patients who had not been on benzodiazepines, suggesting that this class of drugs may cause functional changes in the brain that are permanent or at least slowly reversible.<sup>10</sup> While there is strong evidence that benzodiazepines have negative effects on cognitive performance while using the medication, not all studies support the same conclusion, and research is inconclusive as to how long the damage lasts once the medication is discontinued. A meta-analysis involving 13 studies that lasted for at least one year and were published between 1980 and 2000 examined the effects of long-term benzodiazepine use on cognition.<sup>5</sup> The authors were not able to make conclusions about whether or not the cognition and memory impairment of benzodiazepines extended beyond therapy termination due to the heterogeneity and limited number of studies in the meta-analysis. The study points to the complicated nature of assessing cognition considering the impact of test-induced anxiety in patients who may already be prone to anxiety. In practice, however, the most conservative treatment plan should be used if possible; the potential risk of lingering CNS effects impacting cognition is high enough to discourage long-term use of benzodiazepines if another treatment of equal efficacy is available.

### Motor Vehicle Accidents

Decreased alertness, altered decision-making capacity and changes in perception are cognitive-based factors that contribute to an increased risk of motor vehicle accidents in elderly patients taking benzodiazepines.<sup>14,15</sup> Reaction time is another critical factor that is negatively impacted by benzodiazepine use.<sup>14</sup> Crashes that involve elderly drivers are generally related to perception and cognitive difficulties, such as crossing the center into the adjacent lane, inappropriate judgment of gaps between vehicles and not giving way to other vehicles. Although studies still show that younger drivers are more likely to be in car accidents than older drivers, the risks are highest in those ages 18 to 25 years and ages 65 years and greater.<sup>14,15</sup> Importantly, in the 65 years of age and greater population, there is an even higher risk of accidents in those taking benzodiazepines.<sup>14</sup> In fact, benzodiazepines are commonly found at detectable blood levels in people involved in car accidents when it is suspected that they were impaired due to substances. This finding includes both ben-

zodiazepines being used therapeutically and as drugs of abuse, meaning it includes those taking benzodiazepines for reasons other than prescribed or at doses higher than prescribed. As expected, the risks associated with benzodiazepines and traffic accidents increase with the size of the dose, the number of benzodiazepines being used, combinations with other CNS depressants (e.g., alcohol) and how long the driver has been taking the medication. This may even suggest that tolerance develops to the side effects of the medication with chronic use compared to the cognitive changes seen initially in a patient on a benzodiazepine.<sup>16</sup>

### Physical Disability

Benzodiazepines increase the risk for mobility impairments and difficulties with completing daily tasks such as bathing, dressing and feeding.<sup>3,17</sup> The decline in physical performance is due to the effects on the patient's neuromuscular processing and psychomotor abilities, as well as the sedation, that is caused by benzodiazepine use.<sup>3</sup> Again, there is some natural risk of declining mobility and ability to perform daily tasks associated with aging, but benzodiazepine use in the elderly has been found to increase the risk for physical disability by 23 percent. Specifically, women are at a greater risk for these changes than elderly men likely due to poorer muscle strength and control initially.<sup>3,17</sup> Although it was previously believed that these physical impairments would be lessened if the patient was prescribed short-acting rather than long-acting formulations due to the shorter half-life, not all studies support this theory.<sup>3</sup> Short-acting benzodiazepines are more likely to be taken in higher doses, therefore increasing total drug exposure and leading to higher peak concentrations. Overall, risk for physical disability is greatest in patients using higher doses and long-term therapy, defined as three years or more in this study specifically.<sup>17</sup> Unfortunately, the negative effects on physical functioning can still be seen even at low doses of benzodiazepines.<sup>3</sup> Although higher drug exposure does tend to lead to more detrimental effects, there are still many interindividual differences that allow low doses to have an equally negative impact in some patients. One study examined whether the physical disability was resulting from benzodiazepine use itself or from a shift to a less active lifestyle due to the sedative effects of the medication. It was concluded that activity level was not a confounder in decreasing physical performance, so it can be concluded that the effects of the benzodiazepine were likely the reason for the decline in physical function.

### Fall Risks

Benzodiazepines are one of many drug classes that pose a fall risk in the elderly population owing to an increase in the risks associated with falls, such as impaired muscle strength, coordination and balance. Although risk of falls increases naturally with aging, benzodiazepine use can exacerbate this risk. In a study, handgrip strength and balance were used as indicators to assess fall risk in elderly patients taking the intermediate-acting benzodiazepine, temazepam, or one of two Z-drugs, zolpidem or zolpiclone, which work similarly to benzodiazepines.<sup>18</sup> Successful discontinuation from long-term benzodiazepine use led to an improvement in handgrip strength and balance in elderly patients. The findings showed



that benzodiazepine usage does play a significant role in fall risk, and the incidence among some elderly patients may be due to more than typical age-related decline. This fact increases the importance of identifying patients who could be switched to an alternate therapy. As women are at a greater risk of physical disability than men, as noted earlier, this also places them at a greater risk for falls than men. Considering overall health care economics, benzodiazepines are relatively inexpensive medications, but the financial burden of treating falls and fall-related injuries attributed to benzodiazepine use can be significant.

### Fractures

In the elderly population, fractures and other musculoskeletal injuries are often sustained due to falls. As expected, there is an increase in fractures in long-term benzodiazepine users.<sup>19</sup> Similar to the research regarding physical disability in general, there was not a difference in fractures sustained due to benzodiazepines based on whether they were short-acting or long-acting products.<sup>3,19</sup> In a study that compared the United States with several large European countries, the overall average of hip fractures that could be attributed, at least in part, to benzodiazepine use was 1.8 to 8.2 percent.<sup>19</sup> Although this is a large range, even the most conservative finding of 1.8 percent shows that fractures as a consequence of benzodiazepine use are still meaningful when considering the other age-related and drug-related causes for fractures and falls in the elderly population and the individual impact a fracture has on a patient's quality of life.

### Sleep Problems

Sleep disturbances are a frequent reason for an elderly patient to be prescribed a benzodiazepine, yet approximately 80 percent of the elderly population who are taking benzodiazepines report having problems with sleep.<sup>20,21</sup> Despite the indication for benzodiazepines to help with sleep, a study found that overall sleep quality declined in adults 65 years of age or older when using benzodiazepines long-term.<sup>20</sup> Though these medications are generally only recommended to be used for three months, regardless of age and indication, most patients use them for much longer. Another meta-analysis that examined 45 randomized controlled trials testing benzodiazepine use for insomnia found that although benzodiazepines are slightly beneficial in increasing the length of time a patient is asleep, there are not any significant benefits on the length of time for sleep onset, and there are additional negative effects associated with their use.<sup>21</sup> The most common negative effects patients reported in the studies included being drowsy during the day, dizziness and lightheadedness. For long-term users of benzodiazepines, the risks and negative effects associated with usage outweigh the potential benefit for sleep.

Like most of the effects discussed previously, sleep disturbances are seen more significantly in the elderly population due to the negative impacts of benzodiazepine use being compounded with natural, age-related decline in sleep quality.<sup>20</sup> Importantly, not only did the benzodiazepine users have poorer sleep quality than nonusers, but those taking benzodiazepines long-term had the worst sleep quality overall

when compared to those who only took the medications short-term. This result is not often seen in initial clinical trials assessing medications' effects on sleep because research is often not conducted for a long enough time to appropriately examine the effects of the drug long-term, which is how the drugs are often used in practice.

### Withdrawal

Although cognitive impairment, physical disabilities and sleep problems are possible adverse effects of taking benzodiazepines, withdrawal is perhaps the biggest controversy pertaining to their use. However, due to prescribing traditions and patient preference, long-term use of benzodiazepines occurs in more than one-third of patients.<sup>22-24</sup> This is a cause for alarm due to the risks of adverse effects and continued efficacy. A study by Salzman and colleagues found the memory and cognitive functioning of elderly nursing home patients improved in those tapered off benzodiazepines when compared to those who remained on the medications.<sup>25</sup> The recommendation for those patients on benzodiazepines for longer than three months is to gradually reduce the dosage through a tapering schedule.<sup>26</sup> This taper should last less than six months or else this process occupies all of the patient's focus.<sup>25</sup> Before interrupting benzodiazepine use, health care providers should ensure the patient is in good health, and that he or she is fully educated about the possible recurrent, rebound or new symptoms that can occur.<sup>22,27</sup>

The original indication for benzodiazepine use, whether insomnia or anxiety, may worsen to pretreatment levels during the tapering period.<sup>24</sup> In some cases, the symptoms may elevate beyond pretreatment levels and is considered a rebound symptom. Therefore, it is necessary to evaluate the patient's underlying medical or psychiatric conditions before ceasing benzodiazepine use.<sup>22</sup> Symptoms of withdrawal and rebound are enhanced with the use of short-acting benzodiazepines due to their short half-life, rapid elimination and increased dosing frequency (Table 1).<sup>24</sup> The short-acting agents, midazolam and triazolam, are generally not used throughout the day, so the withdrawal and rebound may not be as evident, although rebound effects have been reported with the use of triazolam.<sup>28</sup> Alprazolam and oxazepam, which are considered intermediate-acting agents with half-lives of about three to 20 hours, may be dosed more frequently and are associated with symptoms of withdrawal and rebound if discontinued abruptly.<sup>27</sup> Rebound symptoms may occur after long-term use of any benzodiazepine, and may require a nonbenzodiazepine substitute for those experiencing exacerbations of their sleep disorders or anxiety. Selective serotonin reuptake inhibitors (SSRIs) or tricyclic antidepressants (TCAs) are acceptable alternatives for those with rebound depressive symptoms, and melatonin agonists, such as ramelteon (Rozerem®), may aid in sleep disorders.<sup>23,25,29,30</sup> Psychological support, spanning from encouragement to cognitive or behavioral therapy, should also be provided for those patients in need of anxiety management and should be available long after tapering is complete.<sup>23</sup> Decreased use of caffeine and alcohol, along with proper sleep, hygiene and relaxation techniques, may be enough to help insomnia without the need to initiate medications. Overall, the entire health

care team needs to be prepared to help the patient pharmacologically and nonpharmacologically with any issues resulting from rebound symptoms throughout tapering.

Along with possible rebound symptoms, withdrawal symptoms add to the difficulty of the benzodiazepine tapering process. The most frequent withdrawal symptoms include insomnia, anxiety, mood swings, myalgia/muscle twitching, tremor, headache, nausea/vomiting, loss of appetite, hypersensitivity to noise, changes in movement and feelings of unreality.<sup>29</sup> Throughout the withdrawal process these symptoms wax and wane and can differ in severity for each patient.<sup>23</sup> The 20-item Benzodiazepine Withdrawal Symptom Questionnaire or the Physician Withdrawal Checklist can be used to measure patient's symptoms during each case of withdrawal.<sup>31</sup> Due to these occasionally unbearable symptoms, slow dosage reduction and proficient psychological support are necessary for the success of benzodiazepine tapering.<sup>23</sup> Abrupt withdrawal could cause convulsions, panic reactions and acute psychotic states. The occurrence of seizures upon withdrawal, although rare, is more likely in patients with an underlying seizure disorder or when receiving concomitant medications that may lower the seizure threshold.<sup>27</sup> As previously mentioned, tapers should last less than six months, but this process should be adapted to each individual patient based on lifestyle, personality, environment and available support.<sup>23,25</sup>

Dosage reduction is an individualized process based on each patient's characteristics.<sup>23</sup> Those on higher doses of benzodiazepines can tolerate larger dosage cutbacks, and the majority of patients take therapeutic doses less than 20 mg diazepam or equivalent daily. The usual dose of diazepam for the treatment of anxiety is 2 mg to 10 mg two to four times daily if needed, allowing for a maximum dose per day of 40 mg.<sup>32</sup> Generally, it is recommended to reduce the dose by 10 percent to 25 percent each week.<sup>22</sup> Reductions of 1 mg diaze-

pam every one to two weeks are usually well tolerated.<sup>22</sup> Yet, if the patient is taking 40 mg of diazepam daily, an initial reduction of 2 mg every one to two weeks may be more appropriate, as the patient is considered to be on a higher dose. Once the daily dosage reaches 4 mg to 5 mg, decreasing by 0.5 mg may be preferred to prevent negative effects. In order to improve adherence and patient's peace of mind, a written withdrawal schedule should be provided rather than just verbal instructions. A chart to check off days and doses is helpful for patients to stay goal-oriented. These schedules will be flexible to changes upon the appearance of any problems, such as severe symptoms or stressors. If at any point in the process withdrawal symptoms become notably severe, the tapering can be slowed. Diazepam, an intermediate-acting agent, is the easiest benzodiazepine for tapering since it has multiple available strengths including 10 mg, 5 mg and 2 mg tablets. Therefore, many patients are switched from their original benzodiazepine medication to an equivalent diazepam dosage (Table 2) especially within one month of complete discontinuation.<sup>22,23,27</sup> Keep in mind, psychological and anxiety management should be provided throughout the entire dosage reduction process.

Benzodiazepine withdrawal is a very complex and taxing process for patients. As a result, it is recommended any patient dependent on benzodiazepines and going through withdrawal attends self-help groups run by ex-benzodiazepine users, psychologists, counselors or trained paramedical workers.<sup>23</sup> Along with these group meetings, it is important for the patients to receive individualized psychological care in which they can confront personal or social problems underlying their anxiety and need for long-term benzodiazepine use. Involvement of family members in this practice is significant because it allows the patient to feel supported and to expose themselves to others, which increases their confidence and self-esteem. These individuals need to be highly self-motivated in order to succeed with the tapering regi-

**Table 2. Benzodiazepine Equivalent Doses.**<sup>22,23,27</sup>

Benzodiazepines	Oral Doses (mg) Equivalent to 10 mg Diazepam
Alprazolam (Xanax)	0.5 - 1
Chlordiazepoxide (Librium)	25
Clonazepam (Klonopin)	0.5
Clorazepate (Tranxene)	15
Diazepam (Valium)	10
Flurazepam (Dalmane)	30
Lorazepam (Ativan)	1 - 2
Oxazepam (Serax)	20
Quazepam (Doral)	20
Temazepam (Restoril)	20
Triazolam (Halcion)	0.25 - 0.5



mens. As stated earlier, it is important to inform patients of the possible problems that can occur during withdrawal and ensure they are dedicated and willing to fully adhere to the program. Health care providers for any patients going through withdrawal or abusing benzodiazepines can educate them regarding the advantages of withdrawal and establish trust with them each step of the way.

Even though psychological support is available to patients throughout benzodiazepine tapering, the withdrawal symptoms may be perceived as too difficult to handle. Several medications have been evaluated as possible withdrawal and symptom-relief aids in order to allow more patients to be successful. Flumazenil is a benzodiazepine partial agonist which normalizes receptor function and has been evaluated for decreasing patients' craving and relapse rates and even reducing the hostile and aggressive behaviors that are often associated with withdrawal.<sup>33,34</sup> A randomized, placebo-controlled study found that when compared to oxazepam, flumazenil can counteract benzodiazepine effects and control benzodiazepine withdrawal.<sup>33</sup> Topiramate and carbamazepine, both anticonvulsants, have also been investigated in the treatment of withdrawal symptoms and possibly relapse prevention.<sup>35</sup> However, none of these medications have been found to be fully successful in preventing benzodiazepine withdrawal.

### Role of the Pharmacist

Long-term use of benzodiazepines can lead to many adverse effects, cognition issues and withdrawal symptoms. As one of the most accessible health care providers, pharmacists can have significant impact by aiding patients throughout this complicated and difficult process. First, pharmacists in all institutions and fields of pharmacy can identify elderly patients taking long-term benzodiazepines and use their professional judgment and knowledge to evaluate if the benefits outweigh the risks for each individual patient. Community pharmacists can assist in drug adherence and patient education by identifying potential drug interactions or adverse reactions, supplying weekly pill dispensers or other compliance aids and administering information about specific drugs.<sup>36</sup> However, the pharmacist's responsibility expands far beyond the patient. Pharmacists are in a good position to communicate with prescribers in both the inpatient and community settings to determine if patients could be switched to another less risky therapy to treat their condition. Also, pharmacists should educate other health care professionals and ensure benzodiazepines are being prescribed only for appropriate conditions when other options are not available. Additionally, information should be exchanged between pharmacists and physicians about medication reviews, prescribing committees, compiling drug formularies, dose reduction regimens and possible ways to deal with benzodiazepine withdrawal.

### Conclusion

Benzodiazepines are a commonly prescribed class of medications in the elderly for anxiety and insomnia. However, long-term use of this class of medications is associated with detrimental effects including cognitive impairment,

sleep disturbances and physical disabilities. These drug-associated effects can lead to an increase in motor vehicle accidents in the elderly patient population as well as an increased fall risk leading to more fractures and a decreased quality of life. Withdrawal is one of the greatest issues with long-term benzodiazepine treatment which can lead to rebound symptoms plus mood swings, tremor, headache, loss of appetite and more. A taper of less than six months is recommended when discontinuing long-term benzodiazepine use. Pharmacists can be beneficial during the tapering process, but also have the professional responsibility to identify inappropriate prescribing and use of benzodiazepines in the elderly population, which could circumvent many of these issues altogether. Overall, the continued use of benzodiazepines in this patient population requires pharmacists to stay updated on appropriate indications, side effects and withdrawal concerns as well as educate other health care professionals when necessary.

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## Assessment Questions

1. Why is the high usage of benzodiazepines especially a concern in the elderly population?
  - A. Elderly patients respond to and metabolize benzodiazepines differently.
  - B. Elderly patients are more likely to be taking multiple medications, which may include other centrally-acting ones.
  - C. Benzodiazepines, as a class, are more expensive compared to other medications with similar indications.
  - D. Two of the above are correct.
2. According to the Beers Criteria, which is not a recommended indication for benzodiazepine use in elderly patients?
  - A. insomnia
  - B. anxiety
  - C. panic disorder
  - D. Two of the above are correct.
3. The increase in the severity of negative side effects with benzodiazepine use in the elderly population is primarily because of \_\_\_\_ changes.
  - A. pharmacokinetic
  - B. pharmacogenomic
  - C. pharmacodynamic
  - D. pharmacoeconomic
4. When considering the impact of benzodiazepines on cognition, which is true?
  - A. Negative effects may extend beyond the duration of therapy.
  - B. Dose is a greater predictor of negative cognitive effects than the length of therapy.
  - C. Both A and B are correct.
  - D. Neither statement is correct.
5. In regard to benzodiazepines and physical function, which is true?
  - A. Women are at a higher risk to suffer from a decline in physical function and fractures.
  - B. Negative effects on physical function are not seen with short-acting benzodiazepines.
  - C. The sedative effects of benzodiazepines decrease the activity level and lead to a decline in physical function.
  - D. Two of the above are true.
6. Although typically used much longer, the recommended length of time for using benzodiazepines is \_\_\_\_\_.
  - A. Six weeks
  - B. Three months
  - C. No more than one year
  - D. There is no recommended length of time; long-term use needs to be monitored.
7. When considering the impact of benzodiazepine use on motor vehicle accidents, which is true?
  - A. Benzodiazepines can have detrimental impacts on driving only when used abusively.
  - B. Due to benzodiazepine use (along with other sedative substances), elderly drivers are the most likely to be involved in a motor vehicle accident compared to other drivers.
  - C. Benzodiazepine use can impair reaction time and alertness of an elderly driver.
  - D. Benzodiazepines have not been found to have a significant impact on motor vehicle accidents.
8. The taper schedule for benzodiazepines should be no longer than:
  - A. Two months
  - B. Four months
  - C. Six months
  - D. One year
9. In regard to the tapering process, the recommended dosage reduction of benzodiazepines per week is:
  - A. 10-25%
  - B. 5-10%
  - C. 25-30%
  - D. 15-35%
10. The benzodiazepine partial agonist that has been evaluated for decreasing patient's craving and relapse rates, normalizing benzodiazepine receptor function and even reducing hostile and aggressive behavior often associated with withdrawal is:
  - A. oxazepam
  - B. topiramate
  - C. carbamazepine
  - D. flumazenil



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**Continuing Education Registration & Evaluation Form**

Program Title: **The Effects of Long-Term Benzodiazepine Use and Withdrawal in the Elderly**  
UAN: 0048-0000-15-209-H01-P CEUs: 0.1

*All information must be printed CLEARLY to ensure accurate record keeping for attendance and the awarding of continuing education credit. You MUST provide your CPE Monitor# and Month and Day of birth to receive credit.*

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Phone: \_\_\_\_\_ Email: \_\_\_\_\_

Check one: Pharmacist  Technician  License #: \_\_\_\_\_ State: \_\_\_\_\_

CPE Monitor #: \_\_\_\_\_ Birthday (MM/DD): \_\_\_\_\_

**Program Content:** Strongly Disagree Strongly Agree

Program Content:	1	2	3	4	5
The program objectives were clear.	1	2	3	4	5
The program met the stated goals and objectives:					
1. Explain how benzodiazepines differentially affect the elderly population in terms of pharmacokinetics and pharmacodynamics.	1	2	3	4	5
2. Discuss specific adverse effects of benzodiazepines in the elderly population and how these adverse effects impact quality of life.	1	2	3	4	5
3. Identify patients who are at highest risk of adverse effects with benzodiazepine use.	1	2	3	4	5
4. Describe symptoms of and possible treatments for patients experiencing withdrawal from benzodiazepines.	1	2	3	4	5
5. Identify ways a pharmacist can improve medication management in the elderly population.	1	2	3	4	5
The program met your educational needs.	1	2	3	4	5
Content of the program was interesting.	1	2	3	4	5
Material presented was relevant to my practice.	1	2	3	4	5
Audio/visual and/or printed materials aided the learning process.	1	2	3	4	5
The program used effective teaching/learning methods.	1	2	3	4	5
The learning assessment activities were appropriate.	1	2	3	4	5
The program showed good objectivity and no commercial bias.	1	2	3	4	5
Would you recommend this program to a colleague?	1	2	3	4	5
What was the most valuable part of this program? _____					

Based on what you have learned what one change do you plan to make in your practice? \_\_\_\_\_

**Speaker Content:** Strongly Disagree Strongly Agree

Speaker Content:	1	2	3	4	5
The speaker was well prepared and knowledgeable about the topic.	1	2	3	4	5
The quality of the speaker was excellent.	1	2	3	4	5
The speaker provided adequate time for questions.	1	2	3	4	5

Comments: \_\_\_\_\_

Suggestion for future programs you would like to see: \_\_\_\_\_

**Answers to Assessment Questions—Please Circle Your Answer**

1. A B C D      3. A B C D      5. A B C D      7. A B C D      9. A B C D  
2. A B C D      4. A B C D      6. A B C D      8. A B C D      10. A B C D

Any questions/comments regarding this continuing education program can be directed to Lauren Hamman, Advanced Administrative Assistant for the Office of Continuing Education (email: [l-hamman@onu.edu](mailto:l-hamman@onu.edu), phone 419-772-2280).



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