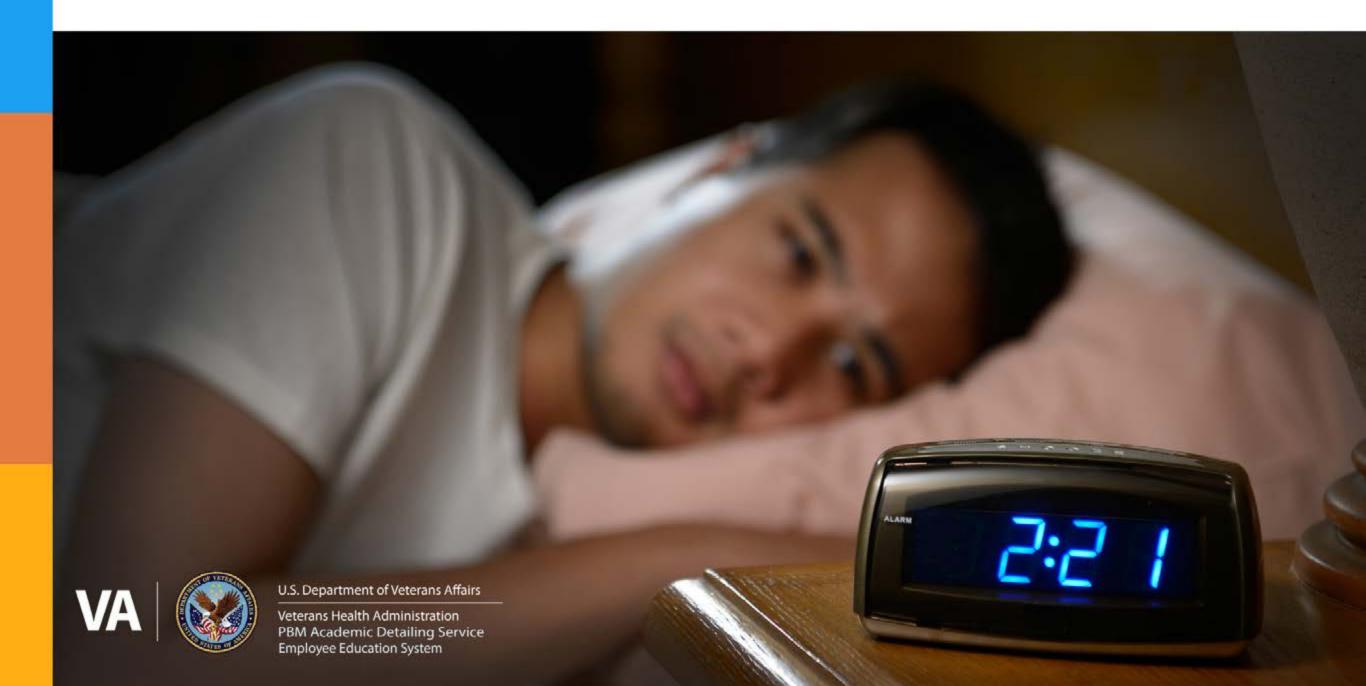
Insomnia Disorder

A VA Clinician's Guide to Managing Insomnia Disorder (2019)



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Insomnia Disorder

Identification and management of insomnia disorder is important to reduce risk for additional conditions and promote overall better health. Studies show that insomnia is a risk factor for hypertension, alcohol use, depression, psychiatric morbidity, suicidality, and increased mortality.^[1-10]

It has also been shown to reduce productivity at work, increase absenteeism, and reduce quality of life.^[2, 14]

Background

Insomnia disorder involves a persistent (occurring for at least three nights per week for at least three months) difficulty with sleep initiation, duration, consolidation, or quality that occurs despite adequate opportunity and circumstances for sleep, and results in some form of daytime impairment. ^[2, 11]

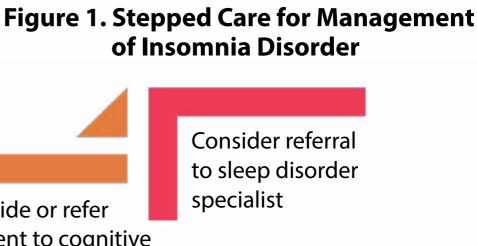
Insomnia is the second most common overall complaint reported in general primary care settings (after pain), with about 30–50% of adults reporting sleep trouble in a given year.^[2]

Diagnose insomnia disorder, if present

Obesity

Provide or refer patient to cognitive behavioral therapy for insomnia (CBT-I)

Complications of Insomnia Psychological problems High blood pressure



Risk of heart

disease

Risk of

diabetes

Identify Veterans who may be suffering from insomnia disorder

Identify Veterans who may be suffering from insomnia disorder

- Ask Veterans if they are having trouble sleeping, such as: difficulty getting to sleep or maintaining sleep, suffering from early-morning awakening, having poor quality sleep, or excessive daytime sleepiness.
- The Insomnia Severity Index (ISI) is a useful screening tool that can be found in MyHealtheVet and in CPRS under the Mental Health Assistant. [12, 13]

Table 1. Brief summary of the ISI^[13]

	Rate the current severity of your insomnia problem(s)					
1	Difficulty falling asleep?					
2	Staying asleep?					
3	Waking up too early?	0	1	2	3	4
4	Satisfied with your sleep pattern?					
5	How noticeable is the impairment in your quality of life from your sleep problem?					
6	How worried are you about your sleep pattern?					
7	How much does your sleep problem interfere with your daily functioning (e.g., daytime fatigue, mood, ability to function at work/daily chores)?					
	Scores from each question can be added to determine level of insomnia					

Scores from each question can be added to determine level of insomnia (e.g., 0-7 = No clinically significant insomnia; 22-28 = Severe clinical insomnia)

Identify Veterans who may be suffering from insomnia disorder

Figure 2. Acute Insomnia to Insomnia Disorder



Acute insomnia symptoms can occur with various medical and psychiatric comorbidities and will sometimes go away on their own with management of the comorbidity or good sleep hygiene (please see the Quick Reference Guide for sleep hygiene guidance).

• If acute insomnia persists for three or more months at a frequency of at least three times per week and meets the above criteria, it is considered insomnia disorder and requires treatment. [1, 2, 11]



Clinical Pearl

Alcohol is often used by Veterans to induce sedation; however, over time, its effect on sleep latency (time it takes to fall asleep) diminishes while sleep disruption persists. This use can lead to a vicious cycle of daytime dysfunction, early morning awakening, insomnia, and increased alcohol use.^[14-16]

Identify Veterans who may be suffering from insomnia disorder

Figure 3. Common causes of sleep disturbance* [1, 6, 17]

Medical comorbidities	 BPH Allergies GERD Migraines Diabetes Pain COPD Hypertension
Sleep disorders	Sleep apneaRestless legs syndrome
Psychiatric disorders	 Depression Anxiety PTSD
Substance use	 Drugs and alcohol Caffeine Nicotine
Medications	 Certain antidepressants (e.g. bupropion, SSRIs/SNRIs) CNS stimulants Opioids Diuretics
Activities/ Psychosocial	 Work schedule Travel Sleep environment Deployments and/or adjusting to civilian life

* This list is not all inclusive. BPH = Benign prostatic hyperplasia, CNS = central nervous system, COPD = chronic obstructive pulmonary disease, GERD = Gastroesophageal reflux disease, PTSD = Posttraumatic stress disorder, SNRIs = Selective serotonin and norepinephrine reuptake inhibitors, SSRIs = Selective serotonin reuptake inhibitors

Diagnose Veterans who may be suffering from insomnia disorder

Make the diagnosis, if present

If the sleep disturbance does not resolve, it is important to evaluate the patient for insomnia disorder and make the diagnosis if insomnia disorder is present.

Table 2. Symptoms and patient behaviors in insomnia disorder^{[11]*}

Symptoms of insomnia disorder	Example patient behaviors	Possible daytime complaints
Difficulty initiating sleep	 Laying in bed for hours but unable to fall asleep Drinking alcohol or using drugs in an attempt to fall asleep 	 Difficulty concentrating Difficulty maintaining attention Difficulty remembering things
Difficulty maintaining sleep	 Waking up multiple times per night due to any number of identifiable factors and/or for unknown reasons Waking one or more times per night and remaining awake for an extended period of time 	 Reduced productivity at work or school Daytime sleepiness
Early morning awakening with inability to return to sleep	 Waking up hours before the alarm is set to go off and being unable to fall back to sleep 	 Low energy or fatigued Mood disturbances (such as mood lability or irritability)

*Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) criteria require a predominant complaint of dissatisfaction with the quality or quantity of sleep, associated with one (or more) of the above symptoms. These symptoms result in clinically significant distress or impairment in social, occupational, educational, academic, behavioral, or other important areas of functioning; problem occurs despite ample opportunity to sleep.

If the patient suffers from insomnia disorder, make the diagnosis and offer treatment.^[17, 18]

Cognitive behavioral therapy for insomnia (CBT-I) is recommended as the first line treatment for insomnia disorder.^[1, 5, 14, 19, 20]

Patients often develop perpetuating behavioral and psychological factors that can lead to further wakefulness, negative expectations, and distorted beliefs about their insomnia.

CBT-I can be used to address these factors.

GOLD STANDARD

Factors that perpetuate sleep problems ^[19, 21-23]

- Irregular bedtime and/or waketime
- Spending excessive time in bed trying to sleep
- Avoidance behaviors during waking hours (e.g., cancelling activities out of fear they will interfere with sleep)



Clinical Pearl

All patients with insomnia disorder should adhere to good sleep hygiene.



Table 3. Components and aims of CBT-I^[23]

Technique	Aims
Stimulus control	If not sleeping, stay out of bed to strengthen bed and bedroom as sleep cues.
Sleep restriction	Limit time in bed to increase sleep drive and consolidate sleep.
Relaxation, buffer, worry time	Reduce arousal.
Cognitive restructuring	Address thoughts and beliefs that interfere with sleep and adherence.
Circadian rhythm entrainment	Shift or strengthen the circadian sleep/wake rhythm.
Sleep hygiene	Address substances, exercise, eating, environment.



CBT-i Coach is an app designed for people who are engaged in Cognitive Behavioral Therapy for Insomnia with a healthcare provider, or who have experienced symptoms of insomnia and would like to improve their sleep habits.

Offering CBT-I to Veterans

Veteran acceptance of CBT-I may be a challenge as not all Veterans may be willing or able to participate; however, many Veterans prefer to use approaches other than medications when they are made available to them.

- Understand what options are available for access to CBT-I
- Consider a shared decision-making approach to discuss this first-line treatment option with Veterans. ^[24]

Table 4. Frequently asked questions and answers regarding CBT-I^[23] Attend six 50 to 60-minute weekly individual or 90-minute group therapy sessions (though some people may improve What does CBT-I require with fewer sessions or need more sessions). from the Veteran? Complete a daily sleep diary and follow recommended treatment guidelines between sessions. Participate in evaluation of progress and determining whether initial goals for treatment were achieved. CBT-I can be tailored for Veterans with varied presentations, including those involving comorbidities. For which patients is • There is empirical support for CBT-I for the treatment of those with insomnia and: **CBT-I most helpful?** * A history of substance use disorder (not active abuse/use) * Psychiatric conditions such as PTSD, depression, bipolar disorder, anxiety disorders, and psychotic disorders * Chronic pain conditions * Other sleep disorders, such as sleep apnea Yes. Some examples are if the Veteran: Are there ever times when Does not meet criteria for insomnia disorder • Is working night or rotating shifts **CBT-I** is not indicated? • Has poorly controlled seizure disorders or severe, unstable psychiatric symptoms. CBT-I can be offered in Primary Care Mental Health Integration (PCMHI) settings Can CBT-I be done and is typically offered as a "brief" course of treatment 4 sessions lasting 15-45 minutes in Primary Care? per session)

Figure 4. Shared Decision-Making for CBT-I ^[24] Tips and example conversation starters				
"Now that we've identified the problem, let's think about what to do next. I'd like us to make this decision together." "There is good information about different treatment options I'd like to discuss with you before we decide on a treatment plan."				
"What treatment options are you familiar with for insomnia?" "Here are some options we can consider" Discuss available treatment options and clearly communicate risks and benefits of each option. Use simple visual aids when possible.				
"As you think about your options, what's important to you?" "When you think about possible risks, what matters most to you?" Use open-ended questions, acknowledge the values and preferences that matter to your patient.				
"Would you like more time to think about your treatment options?" "What questions do you have for me about these options?" "Considering what we've discussed, which treatment option do you think is right for you?				
"Let's plan on reviewing this decision at your next appointment." "If you don't feel like your symptoms are improving, please schedule a follow-up visit so we can discuss the current approach." Patient buy-in is essential!				
e e r				

They are available to partner with you to address your challenges, connect you with local resources, and help improve the care of Veterans.

Provide or refer Veterans with insomnia disorder to CBT-I

Other Clinical Considerations: Pharmacotherapy

If the patient has completed CBT-I but still suffers from insomnia, or if CBT-I is not a good option for that patient, a short pharmacotherapy treatment period of 2 to 4 weeks of intermittent dosing may be considered. ^[1] CBT-I can be considered at any point in treatment.



Clinical Pearl

A 30-day prescription with refills is not needed as extended use is discouraged.

When pharmacotherapy is used, it is important to consider various factors such as: ^[14, 25]

- Symptom pattern (e.g., sleep onset or sleep maintenance difficulties)
- Treatment goals and patient preference
- Past treatment responses

- Availability of other treatments
- Comorbid conditions and contraindications
- Concurrent medication interactions
- Potential adverse effects



Clinical Pearl

Short-term pharmacotherapy should be supplemented with behavioral and cognitive therapies when possible.^[2]

- There are several FDA-approved medications for insomnia; however, most trials are industry sponsored, raising concerns about publication bias.
- Low confidence regarding the overall estimation of risks versus benefits of medications used for insomnia disorder.^[2, 26]
- Potential benefits of medications on sleep quality and daytime function should be balanced against the risk of side effects as well as physical and psychological addiction with long-term use.^[26]



Table 5. FDA-Approved Agents for Insomnia

Listed on the VA National Formulary (VANF)	Not currently listed on VANF
Doxepin Eszopiclone Temazepam Zaleplon* Zolpidem IR, CR*	Ramelteon Suvorexant

*Prior Authorization-Facility (PA-F) medications that are formulary, but require prior approval at the facility level before dispensing.

Table 6. Guideline recommendations for patients with insomnia disorder and no co-morbidities ^[2, 27]

Please note: This figure is based on guidelines that do not consider individual patient characteristics such as comorbidities or drug interactions.

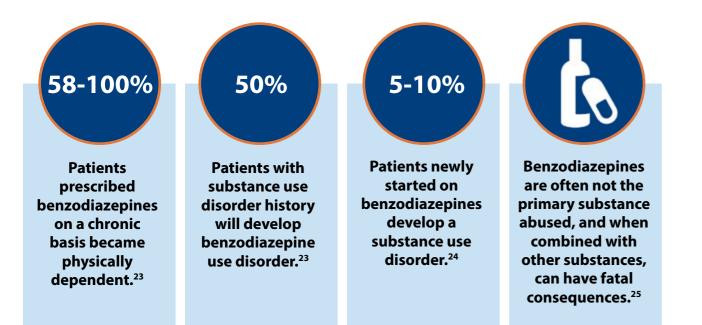
Medication* (listed in alphabetical order)	VA/DoD 2019 CPG Strength of Recommendation	Type of Insomnia	AASM Guideline Strength of Recommendation
Diphenhydramine	Neither for nor against	Sleep onset and/or sleep maintenance insomnia	Not Recommended
Doxepin	Weak for (3 or 6 mg)	Sleep maintenance insomnia	Weak Recommendation
Eszopiclone	Weak for	Sleep onset and/or sleep maintenance insomnia	Weak Recommendation
Ramelteon	Neither for nor against	Sleep onset insomnia	Weak Recommendation
Suvorexant	Neither for nor against	Sleep maintenance insomnia	Weak Recommendation
Temazepam	Weak against	Sleep onset and/or sleep maintenance insomnia	Weak Recommendation
Zaleplon	Weak for	Sleep onset insomnia	Weak Recommendation
Zolpidem	Weak for	Sleep onset insomnia and/or sleep maintenance insomnia	Weak Recommendation

* VA/DoD 2019 CPG considers kava "strong against" and chamomile, melatonin, and valerian "weak against"; AASM = American Academy of Sleep Medicine; CPG = Clinical Practice Guideline

When selecting a medication to use for a patient with insomnia, we often find ourselves with only a few FDA-approved medications, most of which have significant risks for many Veterans and weak evidence to support their use. Consider the following examples:

1. Risks of substance use disorders

Benzodiazepines are widely acknowledged to cause physical dependence, with withdrawal effects possibly seen within as little as 4-6 weeks of continued therapy, and can cause addiction in some. ^[28]

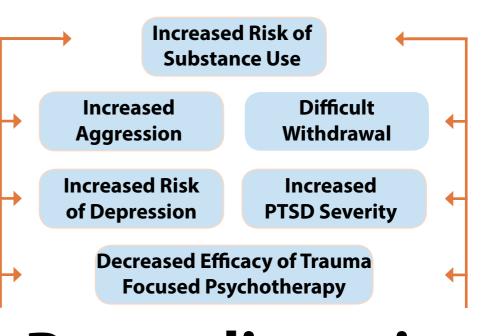


2. Risks in patients with Posttraumatic Stress Disorder

Benzodiazepines are ineffective for the treatment and prevention of PTSD and any potential benefits are outweighed by the risks.^[29-31]

Specific Risks of Benzodiazepine

Use in PTSD

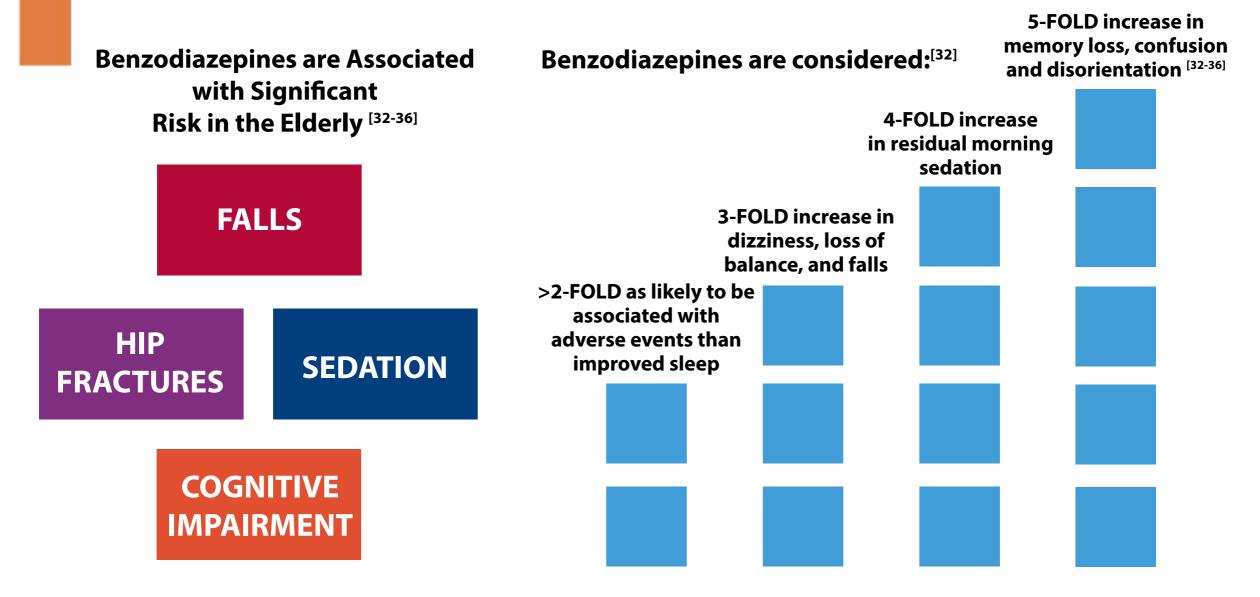


Benzodiazepine



3. Risks in elderly patients and patients with dementia

Sedative hypnotics for the treatment of insomnia have a small magnitude of effect and substantial risk in patients \geq 60 years old. ^[32]



Don't underestimate the risks of some controlled substance medications.





When surveyed about benzodiazepine use, prescribers underestimate the risks in their geriatric patients.^[37]

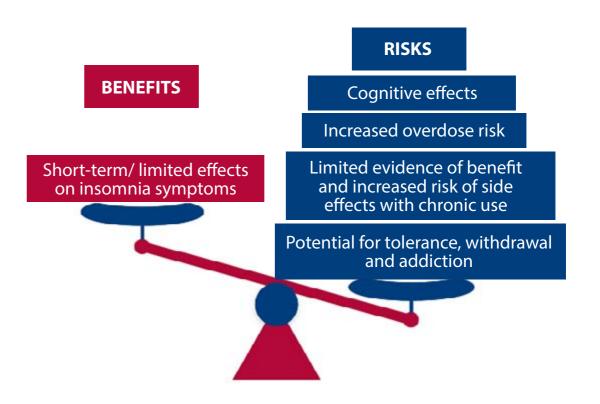
In general, avoid benzodiazepines if the patient:

- Has a substance use disorder
- Has PTSD
- Has a chronic respiratory disease (e.g., sleep apnea)
- Has a history of traumatic brain injury
- Has dementia or is elderly
- Is receiving other CNS depressants such as opioids

Some Provider Perceptions include:

- A stable dose of benzodiazepine means that it is safe and effective.
- Attempts to discontinue will fail.

Figure 5. Weighing the potential risks versus benefits of medication use [38]



Available evidence does not examine the long-term risks of tolerance, withdrawal, difficulty with discontinuation, and addiction in medications used in insomnia disorder. Therefore, we are including information in this brochure about medications without FDA-approved indication for insomnia, but which have some evidence of efficacy and no to low evidence of tolerance and addictive potential.

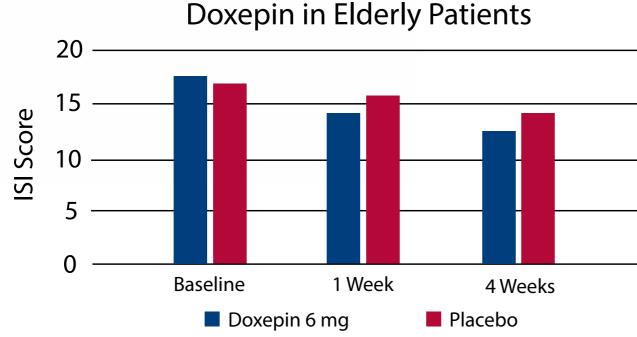
If you would like to consider a medication that is FDA-approved for insomnia and is not a controlled substance, consider the following options:

1. Doxepin

- FDA-approved for insomnia at low doses (3-6 mg)
- Better at sleep maintenance than sleep initiation [39]
- Does not appear to cause significant issues with tolerance or rebound insomnia [40-42]
- Has been shown in various studies to have a side effect profile comparable to placebo^[40, 41, 43-45]
- Use with caution in patients at high risk for suicide due to risk of toxicity in overdose



Figure 6. Doxepin Use^[40]



This randomized double-blind, placebocontrolled trial in 254 elderly outpatients found that low dose doxepin significantly improved total sleep time, wake time after sleep onset, sleep quality, and CGI and ISI scores (all p-values <0.05) compared to placebo.

Doxepin was also shown to be well-tolerated with a side effect profile comparable to placebo (27% incidence of adverse events with placebo vs 31% for doxepin). ^[40]

2. Ramelteon

- FDA-approved for insomnia
- Helps decrease sleep latency but has not been shown to have significant effects on sleep maintenance^[1, 42]
- Does not appear to produce rebound insomnia or symptoms of withdrawal with prolonged use [46]

Many medications are used "off-label" for sleep due to their sedating side effects. These medications may be most appropriate when Veterans have co-morbid psychiatric conditions for which alternative medications have been approved.

Many medications have side effects or other risks that may outweigh the benefits in some patients. It is important to weigh the risks and benefits before selecting an agent.



Trazodone^[39]

- FDA-approved antidepressant
- When used at low doses, it primarily acts at alpha-1, histamine-1, and serotonin-2C and -2A receptors
- There are very few randomized controlled trials evaluating the safety and efficacy of trazodone for insomnia
 - * A small study suggests that low dose trazodone (50 mg at bedtime) improved sleep and did not impair cognition in patients with Alzheimer's disease [47]
 - * A recent study indicates the risk of falls with low-dose trazodone is not statistically different from that of benzodiazepines in nursing home patients age 66 or older (5.7% trazodone, 6.0% benzodiazepines)^[48]
 - * May be an effective sleep aid when used in combination with an antidepressant in patients with depressive disorders^[1, 49]







Mirtazapine

- FDA-approved antidepressant
- At low doses (7.5 15 mg), mirtazapine causes sedation primarily by acting as an histamine-1 receptor antagonist^[41]
- When titrated to therapeutic doses (15 45 mg) mirtazapine has been shown to block serotonin-2 receptors and produce favorable changes in sleep comparable to zolpidem and zaleplon^[50]

Amitriptyline

- FDA-approved antidepressant
- Commonly used at low doses for sleep due to histamine-1, muscarinic-1, and serotonin-2C antagonist activity
- Use caution in patients at risk for suicide due to risk of toxicity in overdose
- Associated with anticholinergic side effects, therefore avoid in elderly patients and others sensitive to these side effects





Gabapentin^[51]

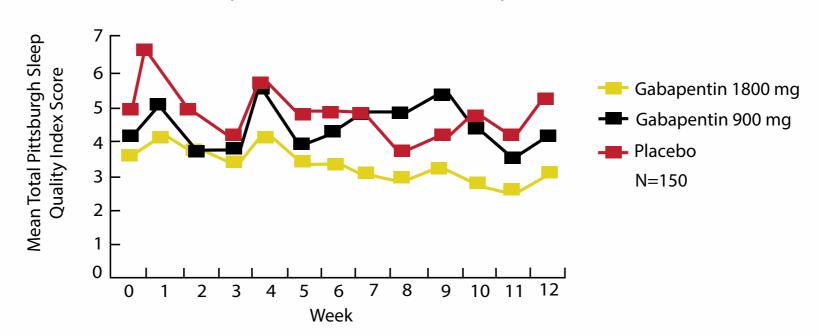
- Has been shown to increase slow-wave sleep (deep sleep), reduce sleep latency, and reduce arousals ^[52]
- May be used to reduce drinking and improve sleep in patients with alcohol use disorders^[51, 53-55]
- Use with caution in patients with a history of substance abuse; potential for psychological and physical dependency exists ^[56]

Antihistamines

(Diphenhydramine, Doxylamine, Hydroxyzine)

- Diphenhydramine and Doxylamine available OTC
- Hydroxyzine may have more profound acute effects on sleep than over-the-counter (OTC) antihistamines^[57]
- Associated with anticholinergic side effects, therefore avoid in elderly patients and others sensitive to these side effects

Figure 7. Gabapentin Use^[51]



Gabapentin and Effects on Sleep



Melatonin

- Available OTC; however, quality of evidence is considered very low and benefits were approximately equal to harms.^[2]
- May be more effective in patients aged 55 and older [58]



Table 7. Sedating Treatment Options for Patients with Co-morbidities⁺

	Pain	Depression	Anxiety Disorder	PTSD	Substance Use Disorder
	Gabapentin	Mirtazapine	Hydroxyzine	Hydroxyzine	Hydroxyzine
	TCA	TCA	Mirtazapine	Mirtazapine	Mirtazapine
Insomnia		Trazodone	TCA	Prazosin*	TCA
			Trazodone	TCA	Trazodone
				Trazodone	Gabapentin**

TCA= tricyclic antidepressant (e.g., amitriptyline, doxepin); +Medications are listed in alphabetical order; *May be considered for patients with trauma-associated nightmares;

**Gabapentin may be effective in reducing alcohol use as well as improving sleep in patients with Alcohol Use Disorder. Gabapentin should be used with caution due to risks of tolerance and dependence.

When managing co-morbidities, ensure the Veteran is being offered or is receiving evidence-based treatment for that co-morbidity (e.g., psychotherapy for PTSD). The schematic below describes risk reduction strategies and recommendations when prescribing medications for insomnia disorder.



Figure 8. Recommendations for Managing Insomnia Disorder When Medications are Being Considered for Short-term Use ^[1, 2, 14, 59, 60]

- Pharmacotherapy should be discussed with patients using a shared decision-making approach, considering:
 - * Treatment goals and expectations; safety concerns; potential side effects and drug interactions; other treatment modalities (cognitive and behavioral treatments); potential for dosage escalation; and rebound insomnia.
- Regular follow-up of patients during the initial period, to evaluate the effectiveness, possible side effects, and need for ongoing medication.
- Try to use the lowest effective dosage of medication and taper medication when conditions allow.
 - * CBT-I can help facilitate tapering/discontinuation of medicines.
- Patients with severe, refractory, and/or chronic insomnia should receive an adequate trial of CBT-I, consistent follow-up, ongoing assessment of effectiveness, monitoring for adverse effects, and evaluation for previously unidentified causes of insomnia, new onset, or exacerbation of existing comorbid disorders.



Risk Reduction Strategy: Tapering and Discontinuing Pharmacotherapy^[1, 61, 62]

- Discontinuing treatment, even if only temporarily, is useful as a strategy to:
 - * Reduce long-term risk of tolerance and adverse effects
 - * Determine if treatment was helpful and whether medication is still needed.
- Tapers can take the form of a dose reduction or a decrease in the number of doses per week.

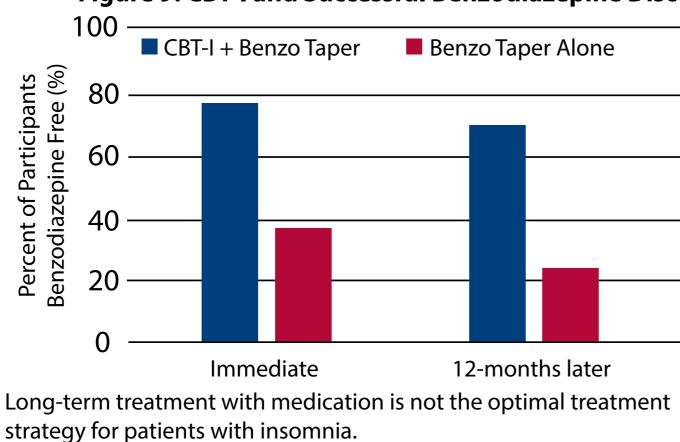


Figure 9. CBT-I and Successful Benzodiazepine Discontinuation^[63]

According to one randomized controlled trial in patients with chronic insomnia, use of CBT-I was strongly associated with being benzodiazepinefree both immediately after treatment as well as at a 12-month follow-up visit.

CBT-I was provided in eight weekly small group sessions. Benzodiazepine tapering was supervised by a physician who met weekly with each participant over the eight-week period.

Results immediately after treatment: 77% (n=34) vs. 38% (n=29), 95% Cl 2.4 – 30.9; at 12-month follow-up: 70% (n=33) vs. 24% (n=29), 95% Cl 2.5 – 26.6.

Consider medication risk reduction strategies and/or tapering whenever possible.



Follow-Up

Consider referral to a sleep disorder specialist

If patients don't respond to initial treatment, consider referral to a sleep disorder specialist: [2]

- To investigate/evaluate:
 - * Clinical suspicion of breathing (sleep apnea) or movement disorders, when initial diagnosis is uncertain
 - * Failure of treatment (behavioral or pharmacologic), or
 - * Precipitous arousals occuring with violent or injurious behavior
- Consideration of other treatment options or combinations





This summary was written by:

Daina L. Wells, Pharm.D., BCPS, BCPP Sarah Popish, Pharm.D., BCPP Julianne Himstreet, Pharm.D., BCPS

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Allen Blaivas, MD Adam Bramoweth, Ph.D. Janet Dailey, Pharm.D. Karen Drexler, MD Philip Gehrman, Ph.D., CBSM Jennifer Martin, Ph.D. Macgregor Montano, Pharm.D. Wilfred Pigeon, MD Ilene Robeck, MD Richard Ross, MD, Ph.D. Michael Saenger, MD, FACP, ADAAPM Todd Semla, MS, Pharm.D., BCGP, FCCP, AGSF Ilse Wiechers, MD, MPP, MHS

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