This is a corrected version of the article that appeared in print.

Treatment of Chronic Insomnia in Adults

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Insomnia affects 30% of the U.S. population, with 5% to 15% meeting criteria for chronic insomnia. It can negatively impact quality of life, decrease productivity, increase fatigue and drowsiness, and put patients at higher risk of developing other health problems. Initial treatment focuses on nonpharmacologic therapies such as cognitive behavior therapy, which improves negative thought patterns and behaviors through sleep restriction, stimulus control, and relaxation techniques. Other nonpharmacologic treatments include exercise, mindfulness, and acupuncture. If these approaches are ineffective, pharmacologic agents may be considered. Medications such as benzodiazepines and Z-drugs are often prescribed for insomnia but should be avoided, if possible, due to short- and long-term risks associated with their use. Melatonin receptor agonists are safer and well tolerated but have limited effectiveness. Dual orexin receptor antagonists are effective in patients who have sleep maintenance insomnia or difficulty with sleep onset. Evidence for the use of antihistamines to treat insomnia is generally lacking, but doxylamine is effective for up to four weeks. (*Am Fam Physician*. 2024;109(2):154-160. Copyright © 2024 American Academy of Family Physicians.)

Approximately 30% of the U.S. population reports experiencing insomnia, with 5% to 15% of the total population meeting the formal criteria for chronic insomnia.[1-3] The American Academy of Sleep Medicine defines insomnia as impairment of the initiation, duration, consolidation, or quality of sleep that occurs despite adequate opportunity for sleep and results in some form of daytime impairment.[4] Chronic insomnia is diagnosed when patients have symptoms at least three times a week for three months or longer.[4,5] Insomnia can have a significant impact on a patient's quality of life, leading to decreased productivity, increased fatigue and drowsiness, and higher risk of developing other health problems.[6,7]

Numerous medical disorders are associated with chronic insomnia, including, but not limited to, hypertension, asthma, chronic obstructive pulmonary disease, obstructive sleep apnea, benign prostatic hyperplasia, chronic pain, gastroesophageal reflux disease, depression, anxiety, posttraumatic stress disorder, and substance use disorders (e.g., caffeine, alcohol, stimulants, opioids).[8,9] To successfully treat chronic insomnia, the care team must address any underlying conditions that may be contributing.

CME This clinical content conforms to AAFP criteria for CME. See CME Quiz on page 111.

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Evaluation and Initial Treatment

A comprehensive evaluation of the patient should include a thorough medical and psychiatric history, a detailed assessment of sleep-related behaviors and symptoms, a physical examination, and laboratory testing as needed. The sleep assessment should include the patient's sleep hygiene regimen. Sleep hygiene practices, such as maintaining a regular sleep schedule, reducing exposure to screens before bedtime, creating a quiet and dark sleep environment, and using the bedroom only for sleep and intercourse, should be implemented. Cognitive behavior therapy for insomnia (CBT-I) is the first-line treatment for chronic insomnia *(Figure 1)*.[10] When nonpharmacologic approaches are ineffective, medications may be considered in the short term (i.e., less than three months), but they should not be used for long-term treatment of insomnia.

Nonpharmacologic Therapies

COGNITIVE BEHAVIOR THERAPY FOR INSOMNIA

CBT-I focuses on changing negative thought patterns and behaviors that contribute to insomnia. It consists of five elements: cognitive restructuring, stimulus control, sleep hygiene, relaxation therapy, and sleep restriction.[11,12] Each

SORT: KEY RECOMMENDATIONS FOR PRACTICE

Clinical recommendation	Evidence rating	Comments
Cognitive behavior therapy for insomnia should be used as first-line treatment for chronic insomnia because it improves the quality of sleep, insomnia severity, daytime fatigue, total sleep time, and beliefs and attitudes about sleep.[3,6,10,11,13,17]	B	Systematic review with meta-analysis of moderate- to low-quality clinical trials with risk of bias and low sample sizes
Mindfulness-based stress reduction can be used to treat insomnia.[6,11]	B	Systematic review of moderate- and lower-quality clinical trials with inconsistent findings
Medications are effective for treating insomnia, but long-term use (i.e., more than three months) is discouraged.[25]	A	Systematic review and meta-analysis of randomized controlled trials
Benzodiazepines and Z-drugs should be avoided when treating insomnia, if possible, due to significant long- and short-term safety concerns.[25,28]	A	Systematic review and meta-analysis of randomized controlled trials

A = consistent, good-quality patient-oriented evidence; B = inconsistent or limited-quality patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to https://www.aafp.org/afpsort.

element can be used individually, but treatment is most effective when all five components are used together. CBT-I has been shown to increase stage N2 (i.e., light sleep, no rapid eye movement [REM]), stage N3 (i.e., deep sleep, no REM), and REM sleep, while decreasing wakefulness and stage N1 sleep (i.e., the first one to seven minutes after a patient first falls asleep), which improves overall sleep architecture.[3,13] CBT-I is particularly helpful for patients with chronic insomnia and comorbid medical conditions, such as chronic pain, depression, posttraumatic stress disorder, cancer, and chronic obstructive pulmonary disease.[14-16] Clinicians with experience in CBT-I can be found through professional organizations such as the Society of Behavioral Sleep Medicine and the American Board of Sleep Medicine.

Through cognitive restructuring, CBT-I addresses maladaptive beliefs and expectations that patients may have to reduce anxiety about inadequate sleep and its consequences. Physicians should set expectations with patients for total sleep duration (5 to 6 hours per night, on average) and focus on supporting daytime function.[17]

Stimulus control reduces stimuli that increase wakefulness before and during sleep time. Patients should associate their beds with only sleep and intercourse, avoid exposure to screens before bedtime, and get out of bed if they are having trouble sleeping.[8]

Sleep hygiene is improved by avoiding naps, caffeine, and alcohol before bedtime and maintaining a stable sleep schedule.[8] The evidence for sleep hygiene alone is weak; the American Academy of Sleep Medicine recommends that the other components of CBT-I be used at the same time.[6]

Relaxation therapy improves self-reported sleep quality, sleep latency, and beliefs and attitudes about sleep.[11]

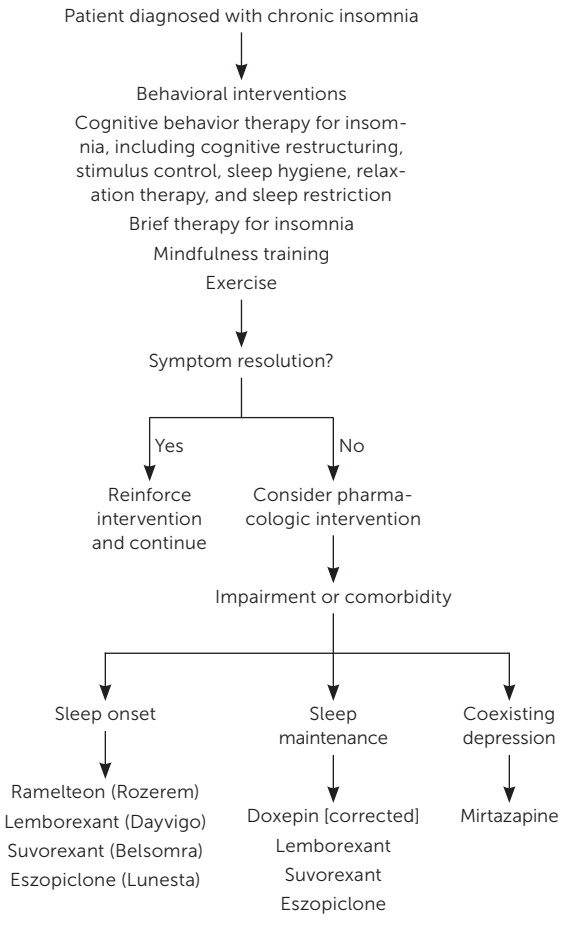
BEST PRACTICES IN SLEEP MEDICINE

Recommendations From Choosing Wisely

Recommendation	Sponsoring organization
Do not offer hypnotics as the only initial therapy for chronic insomnia in adults. Use cognitive behavior therapy for insomnia, whenever possible, and use medications only when necessary.	American Academy of Sleep Medicine
Do not routinely prescribe antipsychotic medications as a first-line intervention for insomnia in adults.	American Psychiatric Association
Do not prescribe benzodiazepines or other sedative-hypnotics in older adults as a first choice for insomnia, agitation, or delirium.	American Geriatrics Society

Note: For supporting citations and to search Choosing Wisely recommendations relevant to primary care, see https://www.aafp.org/pubs/afp/collections/choosing-wisely.html.

FIGURE 1



Note: Behavioral interventions and medications are listed in order of preference.

Treatment of chronic insomnia.

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Relaxation techniques, including progressive muscle relaxation, abdominal breathing, mindfulness, and meditation, reduce mental activity and physical tension before bed.[8]

Sleep restriction is the most effective component of CBT-I. It improves self-reported sleep quality and insomnia severity and reduces the frequency of awakenings.[11] This component increases the drive to sleep by limiting the time allowed for sleep, inducing sleep debt to improve the proportion of time in bed spent asleep and consolidate fragmented sleep. Physicians should ask patients to keep a sleep diary for one to two weeks, then set a consistent wake-up time for getting out of bed with a consistent total time spent in bed. This duration is calculated as the usual total sleep time as perceived by the patient plus 30 minutes, but it must be less than six hours. Sleep restriction is not appropriate for patients with comorbid medical conditions that worsen with sleep deprivation, such as bipolar disorder, seizure disorder, or untreated sleep disorders (e.g., obstructive sleep apnea).[17]

Although evidence is lacking, the American Academy of Sleep Medicine suggests that physicians consider using single components of CBT-I, particularly sleep restriction, for the treatment of chronic insomnia.[6]

OTHER NONPHARMACOLOGIC THERAPIES

Brief therapies for insomnia typically include education about behaviors that improve or interfere with sleep, relaxation techniques, and sleep restriction.[8,18] Brief therapies improve self-reported sleep quality and insomnia severity.[11]

Exercise improves self-reported sleep quality in younger and older adults and may improve sleep efficiency. For patients older than 65 years, muscle endurance training combined with walking is the best type of exercise to improve sleep quality.[19,20]

Mindfulness meditation emphasizes awareness and attention to the present to promote mind and body calmness and relaxation. Mindfulness-based stress reduction teaches meditation through a structured group intervention and mindfulness-based therapy for insomnia. It improves self-reported sleep quality and decreases insomnia severity.[6,11] Mindfulness-based stress reduction is most useful in combination with CBT-I.[21,22]

Meditative movements such as yoga and tai chi may be helpful in improving sleep quality, but data to support these techniques are limited, and results have been mixed.[23]

Verum acupuncture may improve total sleep time, sleep efficiency, nighttime awakenings, and self-reported sleep quality.[24] The evidence supporting acupuncture is limited to verum or traditional acupuncture and requires 12 or more treatments.

Pharmacologic Treatments

When nonpharmacologic approaches are ineffective, medications may be considered. In patients with chronic insomnia, medications may be used alone or in combination with CBT-I, but long-term use (i.e., more than three months) is discouraged.[25] Several common classes of medications are used to treat insomnia *(Table 1)*.[10]

SEDATIVE-HYPNOTIC MEDICATIONS

Benzodiazepines are gamma-aminobutyric acid (GABA) receptor agonists that bind to GABA receptors in neurons, leading to decreased neuronal excitability and causing sedation, decreased anxiety, and muscle relaxation.[26] Five benzodiazepines have been approved by the U.S. Food and Drug Administration (FDA) for treatment of insomnia: temazepam, triazolam, quazepam, flurazepam, and estazolam.[26] Benzodiazepines are associated with a risk

TABLE 1

Comparison of Commonly Prescribed Sleep Medications

Medication	Daily dosage (mg)	Approximate time to peak (hours)	Approximate half-life (hours)	Cost*	Recommended use
Benzodiazepines					
Estazolam	1 or 2	2	15	$25	Sleep onset and maintenance†
Flurazepam	15 to 30	1	74	$20	Sleep onset and maintenance†
Quazepam (Doral)	7.5 to 15	2	55	NA ($877)	Sleep onset and maintenance†
Temazepam	7.5 to 30	1.5	11	$14	Sleep onset and maintenance†
Triazolam	0.125 to 0.25	2	4	$37	Sleep onset†
Z-drugs					
Eszopiclone (Lunesta)	1 to 3	1	6	$20 ($20)	Sleep onset and maintenance†
Zaleplon	5 or 10	1	1	$36	Sleep onset†
Zolpidem	5 or 10	1.6	2.6	$19	Sleep onset and maintenance†
Zolpidem, extended release	6.25 to 12.5	1.5	2.8	$23	Sleep onset and maintenance†
Zolpidem, sublingual	1.75 to 3.5	1	2.5	$85	Night awakening†‡
Anticonvulsants					
Gabapentin	300 to 600	2.5	6	$11	Limited use§
Pregabalin (Lyrica)	50 to 300	3	6	$19 ($600)	Limited use§
Melatonin receptor agonists					
Melatonin	1 to 3	1.5	3.5	$5	Sleep onset
Ramelteon (Rozerem)	8	0.75	2.5	$99 ($405)	Sleep onset
Orexin receptor antagonist					
Daridorexant (Quviviq)	25 to 50	1	8	NA ($513)	Sleep onset and maintenance‖
Lemborexant (Dayvigo)	5 to 10	1	17	NA ($333)	Sleep onset and maintenance‖
Suvorexant (Belsomra)	5 to 20	2	15	NA ($462)	Sleep onset and maintenance‖
Tricyclic and tetracyclic antidepressants					
Amitriptyline	25 to 150	4	30	$10	Limited use¶
Doxepin	3 or 6	3.5	15	$5**	Sleep maintenance
Mirtazapine	7.5 to 15	2	30	$9	Limited use¶
Nortriptyline	25 to 150	8	30	$12	Limited use¶
Trazodone	50 to 100	1	10	$11	Not recommended

continues

NA = not available.

*—Estimated lowest GoodRx price for one month's treatment. Actual cost will vary with insurance and by region. Generic price listed first; brand name price in parentheses. Information obtained at https://www.goodrx.com (accessed December 15, 2023; zip code: 66211).
†—Benzodiazepines and the Z-drugs are recommended for use only in healthy adults for brief periods. They should be avoided in older adults and in patients with a history of substance use disorder or sleep apnea. The use of these drugs has been associated with significant adverse outcomes.
‡—Use only if 3 to 4 hours remain before planned awakening.
§—Off-label use, may consider for insomnia with comorbid seizure disorder, fibromyalgia, restless legs syndrome, or neuropathic pain.
‖—Contraindicated in patients with narcolepsy.
¶—Off-label use, may consider for insomnia with comorbid depression, fibromyalgia, and/or chronic pain.
**—Generic formulation is available in 10-mg capsules ($5 for 30). Although safe, this dosage has not been approved by the U.S. Food and Drug Administration for the treatment of insomnia.
††—Off-label use, may consider for insomnia with comorbid seizure disorder or bipolar disorder.

TABLE 1 *(continued)*

Comparison of Commonly Prescribed Sleep Medications

Medication	Daily dosage (mg)	Approximate time to peak (hours)	Approximate half-life (hours)	Cost*	Recommended use
Antihistamines					
Diphenhydramine	25 to 50	2.5	8.5	$3	Not recommended
Doxylamine	25	2.4	10	$5	Sleep onset and maintenance
Hydroxyzine	50 to 100	2	20	$10	Not recommended
Antipsychotics					
Olanzapine (Zyprexa)	2.5 to 20	6	30	$9 ($490)	Limited use††
Quetiapine	50 to 400	1.5	6	$9	Limited use††
Risperidone	0.25 to 6	1	20	$4	Limited use††

NA = not available.

*—Estimated lowest GoodRx price for one month's treatment. Actual cost will vary with insurance and by region. Generic price listed first; brand name price in parentheses. Information obtained at https://www.goodrx.com (accessed December 15, 2023; zip code: 66211).
†—Benzodiazepines and the Z-drugs are recommended for use only in healthy adults for brief periods. They should be avoided in older adults and in patients with a history of substance use disorder or sleep apnea. The use of these drugs has been associated with significant adverse outcomes.
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||—Contraindicated in patients with narcolepsy.
¶—Off-label use, may consider for insomnia with comorbid depression, fibromyalgia, and/or chronic pain.
**—Generic formulation is available in 10-mg capsules ($5 for 30). Although safe, this dosage has not been approved by the U.S. Food and Drug Administration for the treatment of insomnia.
††—Off-label use, may consider for insomnia with comorbid schizophrenia or bipolar disorder.

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of dependence and have significant adverse effects including daytime sedation, ataxia, falls, cognitive impairment, respiratory depression, rebound insomnia, and anterograde amnesia.[4,27,28]

Z-DRUGS

Nonbenzodiazepine hypnotics are known as the Z-drugs and include zaleplon, zolpidem, and eszopiclone (Lunesta). They are the most prescribed medications for treatment of insomnia. Like benzodiazepines, they bind to GABA receptors, causing hyperpolarization of neuron cells; however, they bind more selectively to subunits on the GABA receptor, targeting the sedative effects of the receptor instead of causing the anxiolytic effect.[29] The Z-drugs are associated with motor vehicle crashes, falls, and fractures.[28] Complex sleep-related behaviors such as sleepwalking and sleep eating can happen and are more likely to occur in patients with a history of sleepwalking. Physicians should prescribe these medications at the lowest dose possible and instruct patients to take the medication close to bedtime. They should not be used in combination with other sedative medications.[29] Of the GABA receptor agonists, eszopiclone has the best evidence for effectiveness in long-term use.[27]

ANTIEPILEPTICS

Gabapentin and pregabalin (Lyrica) are prescribed off-label for insomnia. There is limited evidence to recommend this use, but gabapentin may be useful for patients with insomnia and restless legs syndrome. Adverse effects include daytime sedation, weight gain, and dizziness.[30]

MELATONIN RECEPTOR AGONISTS

Melatonin receptor agonists work by binding to and activating melatonin receptors in the brain, helping to regulate the sleep-wake cycle. Melatonin receptor agonists have a low risk of dependence or abuse and are generally well tolerated.[30] The FDA has approved use of two melatonin receptor agonists: ramelteon (Rozerem) and tasimelteon (Hetlioz).[31] Tasimelteon is FDA approved only for non–24-hour sleep-wake disorder and is extremely expensive. The most common adverse effect is rare daytime sedation. Ramelteon has been shown to have small to moderate benefits for sleep

latency but no significant improvement in total sleep time or wake time after sleep onset.

Over-the-counter melatonin products are not regulated by the FDA, and purity varies widely among products.[32] A meta-analysis showed a small benefit for sleep latency and total sleep time.

Melatonin may be considered a first-line pharmacologic agent for sleep onset in older adults, including hospitalized patients and those in long-term care facilities, starting with a dosage of 0.5 mg per day.[8,33]

DUAL OREXIN RECEPTOR ANTAGONISTS

Orexins are neuropeptides that bind to orexinergic neurons, promoting arousal in areas of the brain. Dual orexin receptor antagonists reversibly bind to orexin receptors, which inhibits activation of the arousal system.[34] This class of medications is effective in patients who have sleep maintenance insomnia or difficulty with sleep onset. The FDA has approved the use of daridorexant (Quviviq), lemborexant (Dayvigo), and suvorexant (Belsomra). A 2020 meta-analysis comparing lemborexant to suvorexant found that both drugs were more effective than placebo for primary sleep measures such as sleep latency and increased total sleep time, but the effect of lemborexant was greater than that of suvorexant.[35] Lemborexant also has the strongest evidence for effectiveness when used for more than four weeks.[25] The most common adverse effect is daytime sedation.[36]

ANTIDEPRESSANTS/ANTIHISTAMINES

Doxepin is a tricyclic antidepressant that functions as a histamine receptor antagonist, enhancing sleep maintenance (i.e., time awake after sleep onset and total sleep time). Doxepin is FDA approved at dosages of 3 to 6 mg per day.[35] [corrected] Several antidepressants are used off-label for the treatment of insomnia, such as trazodone, mirtazapine, amitriptyline, and nortriptyline. Trazodone is not recommended due to a lack of clinically significant benefits. Due to limited evidence, other antidepressants should be considered only if there is another indication to treat a comorbid mental health condition.[25]

Although antihistamines (e.g., diphenhydramine, doxylamine) are FDA approved for insomnia, evidence for effectiveness is generally lacking, except for doxylamine, which is effective for use up to four weeks.[25]

ANTIPSYCHOTICS

Several antipsychotics (olanzapine [Zyprexa], quetiapine, and risperidone) are used off-label for the treatment of insomnia, but the evidence for their use is weak. These medications should be used only if the patient has another indication for treatment of a co-occurring medical condition.[32]

SAFETY CONSIDERATIONS

Benzodiazepines, Z-drugs, and dual orexin receptor antagonists are classified as schedule IV drugs by the U.S. Drug Enforcement Administration. Patients taking these medications should be monitored with periodic urine drug screens to test for drugs of abuse. Additionally, prescription drug monitoring systems should be used to track prescriptions of controlled substances.

This article updates a previous article on this topic by Matheson and Hainer,[10] and other articles by Maness and Khan,[37] Harsora and Kessmann,[38] Ramakrishnan and Scheid,[39] Rajput and Bromley,[40] and Eddy and Walbroehl.[41]

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Data Sources: A search was completed in Essential Evidence Plus, the Cochrane database, and PubMed using the keywords chronic insomnia, cognitive behavioral therapy for insomnia, sleep hygiene, stimulus control, exercise and sleep, relaxation and insomnia, acupuncture and insomnia, sedatives and insomnia, hypnotics and insomnia, antihistamines and insomnia, orexin inhibitors, antidepressants, and insomnia. The search included meta-analyses, randomized controlled trials, and systematic reviews. The Centers for Disease Control and Prevention sources were reviewed for epidemiology data. Search dates: January, February, and March 2023.

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