Sleep Disorders Guideline

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Last guideline approval: February 2015

Guidelines are systematically developed statements to assist patients and providers in choosing appropriate health care for specific clinical conditions. While guidelines are useful aids to assist providers in determining appropriate practices for many patients with specific clinical problems or prevention issues, guidelines are not meant to replace the clinical judgment of the individual provider or establish a standard of care. The recommendations contained in the guidelines may not be appropriate for use in all circumstances. The inclusion of a recommendation in a guideline does not imply coverage. A decision to adopt any particular recommendation must be made by the provider in light of the circumstances presented by the individual patient.
Background

This guideline focuses on the three most common types of sleep disorders:

- **Insomnia**, which is the most common general sleep complaint, and affects the majority of people at least occasionally. It is defined as a condition of unsatisfactory sleep (despite having adequate time and opportunity) that leads to impaired daytime function. Insomnia includes difficulty initiating or maintaining sleep, waking too early, and non-restorative sleep.

- **Obstructive sleep apnea (OSA)**, a sleep disorder that involves repeated airway collapse during sleep, leading to partial or complete cessation of breathing.

- **Restless legs syndrome (RLS)**, a sensory motor disorder characterized by an irresistible urge to move the legs, usually accompanied by an unpleasant or uncomfortable sensation that is relieved by movement. Symptoms are exacerbated by rest and relieved by movement, and worsen during the evening and at night.

**Excluded** from this guideline are other sleep problems, such as parasomnias, narcolepsy, and circadian rhythm disorders. If another sleep disorder is suspected, including acting out dreams, sleepwalking, narcolepsy, shifted sleep schedule (delayed sleep phase, night-shift work), or refractory restless legs syndrome (or periodic limb movements), consider referral to Sleep Medicine.

Initial Assessment

Asking the right questions of a patient with insomnia and/or excessive daytime sleepiness can help identify the underlying cause and determine whether a referral is needed.

- Do you have difficulty falling asleep?
- Do you have difficulty staying asleep?
- Do you have periods of prolonged wakefulness?
  - If yes to any of the above, consider **insomnia**. See page 3.

- Do you snore loudly (louder than talking or loud enough to be heard through closed doors)?
- Has anyone observed you stop breathing frequently during your sleep?
- Do you often feel tired, fatigued, or sleepy during the day?
  - If yes to any of the above, consider **obstructive sleep apnea (OSA)**. See page 6.

- Are you bothered by an abnormal sensation of having to move your legs that is worse in the evening and/or when lying still, and is improved by moving your legs or getting out of bed to move around?
  - If yes, consider **restless legs syndrome (RLS)**. See page 7.
Insomnia

Assessment

Insomnia is a diagnosis of exclusion. Patients who report difficulty initiating sleep, difficulty maintaining sleep, waking too early, or experiencing non-restorative sleep should be assessed to rule out:

- Comorbid medical conditions (e.g., pulmonary disease, heart failure, chronic pain)
- Comorbid psychiatric disorders (e.g., depression, anxiety, post-traumatic stress disorder, substance abuse)
- Other sleep disorders (OSA, RLS, circadian rhythm sleep-wake disorders)

Table 1 lists medications that may interfere with sleep.

- Medication effects on sleep are complex. In general, medications can cause sleep disturbances via:
  - Stimulating or activating properties
  - Changes in sleep architecture (e.g., slow wave sleep and REM suppression)
  - Physiological changes (e.g., increased urination)
- Medication effects on sleep vary greatly by individual. For example, some patients who take fluoxetine report insomnia as an adverse effect, whereas other patients experience daytime somnolence.
- For patients who are having difficulty falling or staying asleep, consider:
  - The time of day the patient takes the medication
  - Whether there is an appropriate alternative
- For patients who are experiencing medication withdrawal effects:
  - Advise the patient that the sleep disturbance is temporary.

<table>
<thead>
<tr>
<th>Drug class</th>
<th>Difficulty falling asleep</th>
<th>Difficulty staying asleep</th>
<th>Medication withdrawal effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Albuterol</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Alpha-receptor agonists</td>
<td></td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Antidepressants: SSRIs, SNRIs, bupropion</td>
<td>X (particularly fluoxetine, venlafaxine, duloxetine, bupropion)</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Beta-blockers</td>
<td></td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Corticosteroids</td>
<td>X</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Diuretics</td>
<td></td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Opioids</td>
<td></td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Stimulants</td>
<td>X</td>
<td>X</td>
<td></td>
</tr>
</tbody>
</table>

Patients should be encouraged to keep a sleep diary for 1 to 2 weeks to help identify sleep-wake times, general patterns, and day-to-day variation. Since it is common for older adults to sleep less deeply and for less time than they did when they were younger, the elderly are at higher risk for sleep problems.
Treatment

Before prescribing medication for insomnia, behavioral treatment—especially sleep hygiene—is recommended.

Behavioral treatment

Behavioral therapy is recommended as the initial treatment for insomnia. There is good evidence that behavioral therapy is effective in treating insomnia and that the improvement gained is long-term.

Behavioral strategies can include:
- Sleep hygiene
- Stimulus control
- Sleep restriction
- Relaxation training
- Cognitive behavioral therapy–insomnia (CBT-I)

Sleep hygiene

Sleep hygiene focuses on teaching good sleeping habits to patients (e.g., keeping a regular schedule, daytime exercise, avoiding napping) and can help to identify and address specific habits, behaviors, and environmental factors that can impact sleep.

Tips for getting a good night's sleep (The SmartPhrases .avs insomnia and .avssleepactionplan are available for after visit summaries.)

Here are some tips that can help you get a good night's sleep without having to use medicine.
- Create a bedtime routine. Get ready for bed, get into bed, and get up at the same time every day, even on weekends. Establishing a routine helps regulate your inner clock. Try not to take naps during the day.
- Take time to relax before getting into bed. Doing something you enjoy, like reading, taking a warm bath, or using other relaxation techniques can reduce stress and quiet your mind for sleep.
- Your bedroom should be cool, dark, and quiet for sleeping. If street lights shine in your room, or you need to sleep during the day because of your work schedule, put room-darkening shades, blinds, or drapes on the windows.
- Your bedroom should be as quiet as possible. If you can’t block outside noise, cover it up with a familiar inside sounds, like the steady hum of a fan.
- Move the clock away from your bed, so you can’t see it easily. Try putting it under your bed so you can still hear the alarm when it goes off.
- If you share your room or bed with someone who is restless, snores, keeps the light on late for reading, or steals your covers, make arrangements to sleep separately until you establish a regular sleeping pattern.
- Only use your bedroom for sleeping and sexual activity. Don’t use your bedroom for working, having discussions, watching TV, or using your computer.
- Avoid too much mental or physical stimulation an hour or so before going to bed. Don’t finish office work or get into a big discussion about finances or other stressful topics right before getting ready to sleep.
- Get some exercise each day. You might find that exercising 3 to 4 hours before going to bed helps you to sleep better. However, don’t exercise vigorously later than 3 hours before your bedtime.
- Follow a healthy diet. Don’t drink beverages that have caffeine, even soft drinks, after 2 p.m. Drinking alcohol, using tobacco, and taking certain medicines can also make it hard to fall asleep. If you drink alcohol before bed, you might have periods of wakefulness during the night, after the alcohol wears off.
- If, after 30 to 45 minutes of trying, you have trouble falling asleep or getting back to sleep, get up and leave the room for a while. Doing something relaxing in another room, such as reading, might help you feel sleepy so you can go back to bed.
**Stimulus control**
Stimulus control helps the patient to form a positive and clear association between the bed and sleep and to establish a stable sleep-wake schedule.

**Sleep restriction**
Sleep restriction initially limits the time in bed to the total sleep time, as derived from baseline sleep logs. This approach is intended to improve sleep continuity by using sleep restriction to enhance sleep drive. When sleep continuity substantially improves, time in bed is gradually increased.

**Cognitive behavioral therapy – insomnia (CBT-I)**
CBT-I is a combination of cognitive therapy and behavioral treatments, with or without relaxation training. The goal is to change unrealistic expectations and negative thoughts about sleep. While patients who are interested in CBT-I may be referred to BHS for treatment, availability is limited.

**Pharmacologic treatment**
If behavioral treatment has been ineffective, short-term pharmacologic treatment may be considered. Tables 2 and 3 provide information on dosing, potential benefits, and safety considerations for the most commonly used medications for sleep; over the counter (OTC) medications (e.g., melatonin), benzodiazepines and Z-drugs (e.g., zolpidem), and sedating antidepressants (e.g., trazodone).

Both benzodiazepines and Z-drugs are effective in the relief of short-term (1–2 weeks) but not long-term insomnia. The treatment period should not exceed 2 weeks, as sleep studies have shown that sleep patterns return to pre-treatment levels after only a few weeks of regular use. Note: Z-drugs are not “safer” than benzodiazepines, and patients on benzodiazepines should not be switched to Z-drugs to try to improve safety. (See the Benzodiazepine and Z-drug Safety Guideline and the Drug Alerts on next-day sedation with zolpidem and eszopiclone, available on the staff intranet.)

- Antidepressants show the greatest improvement in sleep length.
- Improvement in sleep latency is similar for all pharmacologic options.

The gui
# First-line acute pharmacologic options

<table>
<thead>
<tr>
<th>Medication</th>
<th>Category</th>
<th>Initial dose</th>
<th>Older adult dose</th>
<th>Max. dose</th>
<th>Sleep latency</th>
<th>Sleep length</th>
<th>Safety considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Melatonin</td>
<td>OTC - supplement</td>
<td>3 mg</td>
<td>3 mg</td>
<td>5 mg</td>
<td>7 min</td>
<td>8 min</td>
<td>No data on long-term use</td>
</tr>
<tr>
<td>Mirtazapine</td>
<td>Antidepressant</td>
<td>15 mg</td>
<td>7.5 mg</td>
<td>45 mg</td>
<td>10 min</td>
<td>80 min</td>
<td>CNS depression, weight gain</td>
</tr>
<tr>
<td>Doxepin</td>
<td>Antidepressant</td>
<td>3–6 mg (10 mg/mL oral solution)</td>
<td>3–6 mg (10 mg/mL oral solution)</td>
<td>10 mg</td>
<td>10 min</td>
<td>80 min</td>
<td>HRME (Limit &lt; 6 mg if ≥ 65.)</td>
</tr>
<tr>
<td>Trazodone</td>
<td>Antidepressant</td>
<td>25–50 mg</td>
<td>25–50 mg</td>
<td>200 mg</td>
<td>10 min</td>
<td>80 min</td>
<td>Orthostatic hypotension</td>
</tr>
<tr>
<td>Diphenhydramine</td>
<td>OTC - antihistamine</td>
<td>25 mg</td>
<td>12.5 mg</td>
<td>50 mg</td>
<td>No change</td>
<td>11 min</td>
<td>HRME Limit use to 2–3 days. May impair physical or mental abilities</td>
</tr>
<tr>
<td>Doxylamine</td>
<td>OTC – antihistamine</td>
<td>25 mg</td>
<td>12.5 mg</td>
<td>25 mg</td>
<td>Not available</td>
<td>Not available</td>
<td>HRME Limit use to 2–3 days. May impair physical or mental abilities</td>
</tr>
</tbody>
</table>

1 Pharmacologic therapy is recommended for intermittent short-term use only.  
2 Doses are daily before bedtime.  
3 Reduction from placebo.  
4 Increase from placebo.  
5 HRME = high-risk medication in the elderly.

### Second-line acute pharmacologic options

<table>
<thead>
<tr>
<th>Medication</th>
<th>Category</th>
<th>Initial dose</th>
<th>Older adult dose</th>
<th>Max. dose</th>
<th>Sleep latency</th>
<th>Sleep length</th>
<th>Safety considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Temazepam</td>
<td>Benzodiazepine</td>
<td>15 mg/day (preferred)</td>
<td>7.5 mg</td>
<td>30 mg</td>
<td>15 min</td>
<td>33 min</td>
<td>All: Unawareness of activities during sleep (e.g., driving)</td>
</tr>
<tr>
<td>Zolpidem</td>
<td>Z-drug</td>
<td>Men: 5–10 mg</td>
<td>Not recommended in adults ≥ 60</td>
<td>10 mg</td>
<td>22 min</td>
<td>11 min</td>
<td>HRME Risk of next-day impairment, unawareness of activities during sleep (e.g., driving)</td>
</tr>
</tbody>
</table>

1 Pharmacologic therapy is recommended for intermittent short-term use only.  
2 Doses are daily before bedtime.  
3 Reduction from placebo.  
4 Increase from placebo.  
5 HRME = high-risk medication in the elderly.  
6 Women are at greater risk of impairment.

Prescribing notes for Tables 2 and 3 on the following page.
Prescribing notes for Tables 2 and 3

Contraindications

- Doxepin is contraindicated during use of MAO inhibitors (MAOIs) and with glaucoma or urinary retention.
- Mirtazapine and trazodone are contraindicated during use of MAOIs, linezolid, or IV methylene blue.
- Temazepam and lorazepam are contraindicated in acute narrow-angle glaucoma; sleep apnea or severe respiratory insufficiency; and intra-arterial injection of parenteral formulations.
- Do not use zolpidem in patients with obstructive sleep apnea or impaired respiratory function.

Pregnancy

- Diphenhydramine and doxylamine are both safe for use in pregnancy.
- Limited human data suggests a low risk for birth defects with mirtazapine, doxepin, and trazodone.
- Limited human data suggests possible risk of oral cleft with temazepam. Additionally, there is a risk of withdrawal in the newborn when temazepam is used during the third trimester.
- Human data suggests no increased risk of birth defects with zolpidem; however, there is an indeterminate risk for preterm birth, low birth weight, and small size for gestational age.
- For additional information, consult:
  - Gerald G. Briggs et al. Drugs in Pregnancy and Lactation (e-book available through the Medical Library)
  - Micromedex—Reprotox and Teris databases

Referral

Consider a referral to Behavioral Health for any of the following:

- Patient is interested in cognitive behavioral therapy.
- Patient exhibits significant anxiety and/or depression, in addition to insomnia.
- Patient is using alcohol or illicit drugs to help with sleeping.

Consider a referral to Sleep Medicine if another sleep disorder is suspected, including acting out dreams, sleepwalking, narcolepsy, or shifted sleep schedule (delayed sleep phase, night-shift work)
Obstructive Sleep Apnea

Assessment and referral

Snoring is common, and not all patients who snore will have sleep apnea.

For patients with snoring and/or witnessed apneas, consider a Sleep Medicine referral if at least one of the following is present:

- Unexplained, excessive daytime sleepiness, which can include falling asleep while driving; unplanned and/or uncontrolled napping; or sleepiness interfering with work or other functioning.
- Unexplained pulmonary hypertension, secondary polycythemia, or resistant hypertension.
- Cardiovascular issues (hypertension, ischemic heart disease, or cerebrovascular disease) for which OSA would be a concerning additional comorbidity.
- Patient is in a mission-critical occupation, such as bus driver, trucker, or pilot.

In Epic, use Ref Sleep Disorder (OSA).

Patients with snoring and/or witnessed apneas but none of the other symptoms/factors listed above might not need a referral to Sleep Medicine. For these patients, management suggestions could include the following:

- Weight loss, as appropriate.
- Change of sleeping position. Snoring and sleep apnea are usually worse when patients sleep on their backs; sleeping on their side instead may help.
- Monitoring for the development of excessive daytime sleepiness or other factors that would merit referral to Sleep Medicine.

The SmartPhrase .avssnoring is available as an after-visit summary.
Restless Legs Syndrome (RLS)

Assessment

Diagnosis
RLS is highly likely in patients who meet all of the following conditions.

- An urge to move the legs that:
  - Is usually accompanied or felt to be caused by uncomfortable sensations in the legs,
  - Begins or worsens during rest or inactivity,
  - Is partially or totally relieved by movement such as walking or stretching, at least as long as the movement continues, and
  - Is worse in the evening than during the day
- The occurrence of the above symptoms cannot be solely accounted for by another medical or behavioral condition. RLS may be confused with a variety of conditions that are associated with leg pain, such as peripheral neuropathy, lumbosacral radiculopathy, myalgia, arthritis, leg cramps, neurogenic or vascular claudication, or akathisia.
- The above symptoms cause significant distress or impairment in social, occupational, educational, or other important areas of functioning.

Further assessment
Check patient’s serum ferritin levels; if less than 50 mcg/L, consider iron supplementation.

Review the list of medications the patient is currently taking. Medications such as antidepressants and lithium may exacerbate RLS. Withdrawal from many drugs—including barbiturates, anticonvulsants, and benzodiazepines—may also worsen RLS.

Treatment
Before considering pharmacologic treatment, consider a short trial of compression stockings to reduce symptoms in patients with adequate lower-extremity circulation (ankle brachial index greater than 0.8). Compression stockings should be avoided in patients with arterial disease.

There is high-strength evidence that the following medications help to reduce symptoms in the short term, but there is insufficient evidence to determine their long-term effectiveness. (Continued on next page.)
### Table 4. Pharmacologic options for restless legs syndrome

<table>
<thead>
<tr>
<th>Medication</th>
<th>Category</th>
<th>Initial dose</th>
<th>Max. dose</th>
<th>Safety considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pramipexole</td>
<td>Dopamine agonist</td>
<td>0.125 mg ^1</td>
<td>0.5 mg ^1</td>
<td>Behavioral disorders including gambling and compulsive shopping are frequently reported. FDA investigating potential increased risk of heart failure</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(May be doubled every 4–7 days, up to 0.5 mg.)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ropinirole</td>
<td>Dopamine agonist</td>
<td>0.25 mg ^1</td>
<td>4 mg ^1</td>
<td>Behavioral disorders including gambling and compulsive shopping are frequently reported.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(May be increased to 0.5 mg after 2 days, 1 mg after 7 days, then by 0.5 mg weekly)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gabapentin</td>
<td>Alpha-2-delta ligand</td>
<td>300 mg ^1</td>
<td>1,800 mg</td>
<td>May cause dizziness or drowsiness</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(Titrate every 2 weeks until symptoms subside, use divided doses three times daily.)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Mild/Intermittent**

<table>
<thead>
<tr>
<th>Medication</th>
<th>Category</th>
<th>Initial dose</th>
<th>Max. dose</th>
<th>Safety considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbidopa/levodopa SR</td>
<td>Dopamine precursor</td>
<td>12.5/50 mg ^1</td>
<td>25/100 mg ^1</td>
<td>Only for mild or intermittent symptoms due to augmentation of RLS symptoms</td>
</tr>
</tbody>
</table>

^1 Dose administered once daily 2–3 hours before bedtime.

**Prescribing notes for Table 4.**
Carbidopa/levodopa causes augmentation of restless legs syndrome with symptoms increasing proportionally at increased doses. Thus, carbidopa/levodopa should only be used initially at low doses for mild and intermittent restless legs syndrome to avoid augmentation.

*Contraindication*
Carbidopa/levodopa SR is contraindicated with use of MAOIs or with narrow-angle glaucoma.

**Referral**
Patients with refractory restless legs syndrome should be referred to Neurology or Sleep Medicine for further evaluation and treatment.
Evidence Summary/References

To develop the Sleep Disorders Guideline, the guideline team has adapted the following externally developed evidence-based guidelines:

**Insomnia**

**Obstructive sleep apnea**

**Restless legs syndrome**
Guideline Development Process and Team

Development Process
The guideline team developed the Sleep Disorders Guideline using an evidence-based process, including systematic literature search, critical appraisal, and evidence synthesis. For details, see Evidence Summary and References.

This edition of the guideline was approved for publication by the Guideline Oversight Group in February 2015.

Team
The Sleep Disorders Guideline development team included representatives from the following specialties: behavioral health, family medicine, nursing operations, pharmacy, and pulmonology/sleep medicine.

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Disclosure of conflict of interest
Kaiser Permanente requires that team members participating on a guideline team disclose and resolve all potential conflicts of interest that arise from financial relationships between a guideline team member or guideline team member's spouse or partner and any commercial interests or proprietary entity that provides or produces health care-related products and/or services relevant to the content of the guideline.

Team members listed above have disclosed that their participation on the Sleep Disorders Guideline team includes no promotion of any commercial products or services, and that they have no relationships with commercial entities to report.