Pharmacy Pearls

September 2025

Key Highlights on the Management of Insomnia

Contributors: Samantha Heacock, PharmD, BCACP, BC-ADM
Contact: AHPPharmacist@urmc.rochester.edu

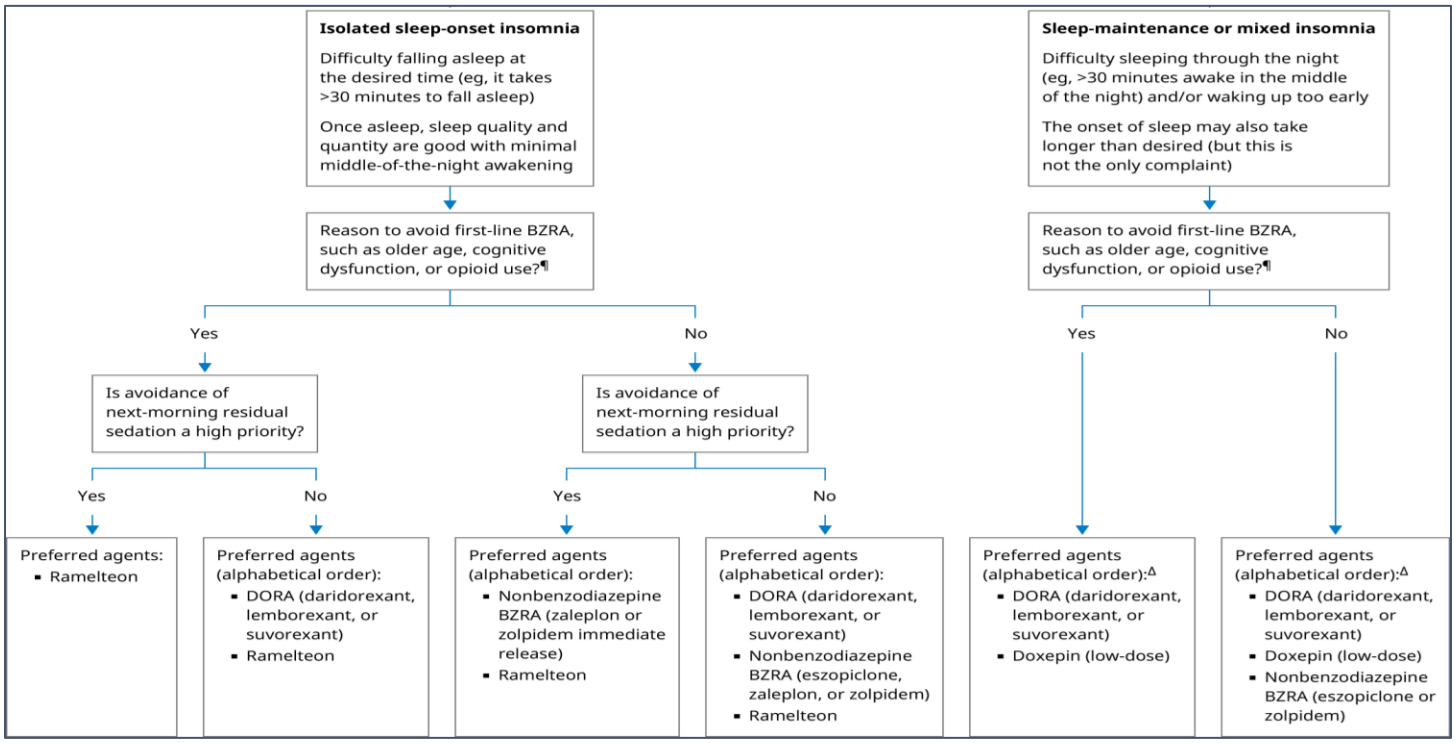
Diagnosis of chronic insomnia: Symptoms occurring at least 3 times per week for ≥3 months

General Considerations for the Treatment of Insomnia:

- 1st line: Non-pharm treatment
  - Cognitive Behavioral Therapy x 4-8 sessions
    - Especially for patients with PTSD
  - Sleep hygiene
  - Discontinue any medications that could contribute to insomnia
- 2nd line: Drug therapy (best if combined with non-pharm methods)
  - Do NOT use OTC products long-term
    - Diphenhydramine, doxylamine
  - Different drugs used for sleep onset vs. sleep maintenance
  - Non-Benzodiazepines preferred long-term

Acetylcholinesterase inhibitors, Alcohol, Antiretrovirals (Emtricitabine, INSTIs), Aripiprazole, Atomoxetine, Bupropion, Decongestants, Diuretics, Fluoxetine, Steroids, Stimulants, and Varenicline

Pharmacotherapy for Insomnia in Adults:



Natural Products:

- Melatonin (3-5 mg in the evening)
  - Indication: Jet lag
  - Can cause additive side effects if used with other CNS depressants
  - Substrate of CYP1A2 → prolonged effects with CYP1A2 inhibitors (ciprofloxacin, fluvoxamine)
- Chamomile tea – may help patients feel calmer

See Page 2-3 for details and clinical pearls on prescription sleep medications

Nonbenzodiazepine benzodiazepine receptor agonists (BZRAs) (C-IV): Increase GABA (inhibitory neurotransmitter)			
Drug	**Dosing**	**Side Effects**	**Clinical Pearls**
Eszopiclone (Lunesta®)	1–3mg po QHS Start 1 mg before bed and increase to 2mg and 3mg PRN	**BBW:** complex sleep behavior (sleepwalking, sleep-driving, engaging in other activities while not fully awake) and lead to serious injury or death **Contraindications:** History of complex sleep behavior **Warnings:** • Increased risk of CNS depression, respiratory depression, and hazardous sleep related activities (sleep-driving) **Side Effects:** • Dysgeusia (eszopiclone only) • Somnolence • Dizziness • Ataxia (clumsy) • Headache • Parasomnias (unusual actions while sleeping) • Lightheadedness • "Pins and needles" feeling on the skin	Not recommended in pregnancy **Counseling points:** Do not take with fatty food or alcohol **Caution when used with CYP3A4 inhibitors:** • Protease inhibitor • Ketoconazole • Itraconazole • Erythromycin • Clarithromycin If used with sedating drug, can cause additive effect (*pain medication, muscle relaxant, anti-histamine, mirtazapine, trazodone, alcohol*) *Potential for dependence (C-IV)* **can cause withdrawal symptoms if used longer than 2 weeks* ***prefer over benzo → lower abuse*
Zolpidem (various formulations): **Ambien®, Ambien CR®** • IR and ER Tablets **Zolpimist™** • Oral spray (5mg/spray) **Edluar®, Intermezzo®** • SL Tablets	**Ambien®, Edlua®, Zolpimist™:** 5–10 mg po/SL/spray QHS **Ambien CR®:** 6.25–12.5 mg po QHS **Intermezzo®:** 1.75–3.5mg SL QHS Start with lowest dose in females and elderly		
Zaleplon (Sonata®)	5–20mg po QHS		

Dual Orexin Receptor Antagonist (DORA) (C-IV): Inhibits orexin neuropeptide → signal that promotes wakefulness			
Drug	**Dosing**	**Side Effects**	**Clinical Pearls**
Lemborexant (DayVigo®) **T ½ = 17-19 hrs (Long)**	5–10mg po QHS Use 5mg with weak CYP3A4 inhibitors	**Contraindications:** Narcolepsy, severe hepatic impairment **Warnings:** • Worsening depression/ suicidal ideation • Sleep paralysis • Hallucinations • Cataplexy-like symptoms (sudden loss of muscle tone) • Increased risk for complex sleep behaviors • Daytime impairment (risk increases if used with other CNS depressants) **Side Effects:** • Somnolence • Headache • Dizziness • Abnormal dreams	Pregnancy: Side effects observed in animal studies (DayVigo® has ongoing study) **Counseling points:** Take on an empty stomach (food delays absorption) within 30 minutes of bedtime and with at least 7 hours of planned sleep time before awakening. • Avoid used with strong or moderate CYP3A4 inhibitors
Suvorexant (Belsomra®) **T ½ = 12 hrs (Intermediate)**	10–20mg po QHS Use 5mg with *moderate CYP3A4* inhibitors; do not exceed 10mg daily		
Daridorexant (Quviviq™) **T ½ = 8 hrs (Intermediate)**	25–50mg po QHS Child Pugh Class B: max 25mg/day		

<table>
<tr><th colspan="4">Melatonin Receptor Agonists: MT1 and MT2 → Promotes sleepiness and regulates the circadian rhythm</th></tr>
<tr><th>Drug</th><th>Dosing</th><th>Side Effects</th><th>Clinical Pearls</th></tr>
<tr><td>Ramelteon (Rozerem®)

T ½ = short (1-2.6 hrs)</td><td>8 mg po QHS</td><td rowspan="2">Somnolence
Dizziness</td><td rowspan="2">Pregnancy: Side effects were observed in some animal studies

Counseling points: Do not take with fatty foods

Interactions: Fluvoxamine (increases serum concentration of ramelteon)

Hetlioz LQ™ may be used in children as young as 3 years</td></tr>
<tr><td>Tasimelteon
Hetlioz®: non-24-hour sleep wake disorder
Hetlioz LQ™: oral suspension
T ½ = short (1-2 hrs)</td><td>20 mg po QHS</td></tr>
<tr><td colspan="4">Tricyclic Anti-depressants: Inhibit norepinephrine and 5-HT reuptake and block acetylcholine and histamine receptors which contributes to somnolence
Silenor® is the brand name of generic doxepin that is FDA-approved for insomnia
Generic doxepin, trazodone, mirtazapine → can be used off-label for sleep though it is not recommended in guidelines</td></tr>
<tr><th>Drug</th><th>Dosing</th><th>Side Effects</th><th>Clinical Pearls</th></tr>
<tr><td>Doxepin (Silenor®)

T ½= 15 hrs (long)

Off-Label (not recommended):
Trazodone and mirtazapine</td><td>3–6 mg PO QHS

If > 65 yo: 3mg</td><td>BBW: Increase in suicidal thoughts or actions in children, teens, young adults within the first few months

Contraindications: MAO-I → 14-day wash out period required

Side Effects:
Somnolence
Anticholinergic SE</td><td>Pregnancy: can use if patient is starting treatment for MDD, but studies are lacking</td></tr>
<tr><td colspan="4">Benzodiazepines (C-IV): Enhance GABA → CNS depression</td></tr>
<tr><th>Drug</th><th>Dosing</th><th>Side Effects</th><th>Clinical Pearls</th></tr>
<tr><td>Temazepam (Restoril™)

T ½= 8-15 hrs</td><td>7.5–30mg po QHS</td><td rowspan="5">Potential for dependence (C-IV)
*can cause withdrawal symptoms if used longer than 2 weeks

Warnings:
Complex sleep behaviors (sleep-driving)
Higher chance of rebound insomnia and daytime anxiety (triazolam)
Contraindications (estazolam and triazolam): do not use with CYP3A4 inhibitors (azole antifungals, protease inhibitors)

Side Effects:
Drowsiness
Dizziness/increase falls risk
Cognitive impairment</td><td rowspan="5">Pregnancy: Crosses the placenta (teratogenicity)

BEERs Criteria: Avoid > 65 years old</td></tr>
<tr><td>Estazolam

T ½= 10-24 hrs</td><td>1–2 mg po QHS</td></tr>
<tr><td>Quazepam (Doral®)

T ½= 39 hrs</td><td>7.5–15mg po QHS</td></tr>
<tr><td>Flurazepam

T ½= 40-114 hrs</td><td>15–30 mg po QHS</td></tr>
<tr><td>Triazolam (Halcion®)

T ½= 2-5 hrs</td><td>0.125–0.5 mg po QHS</td></tr>
</table>