

Insomnia Disorder

A Quick Reference Guide (2019)

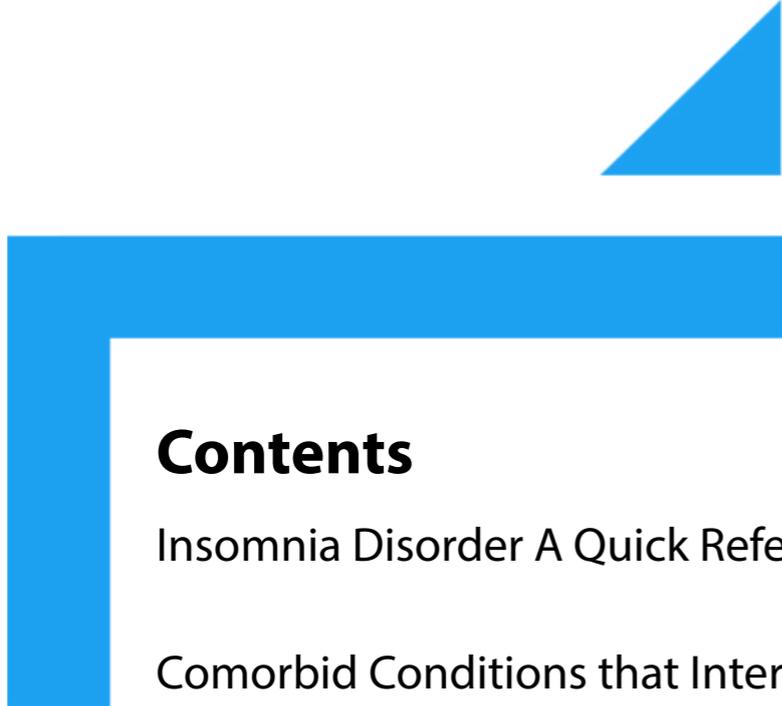


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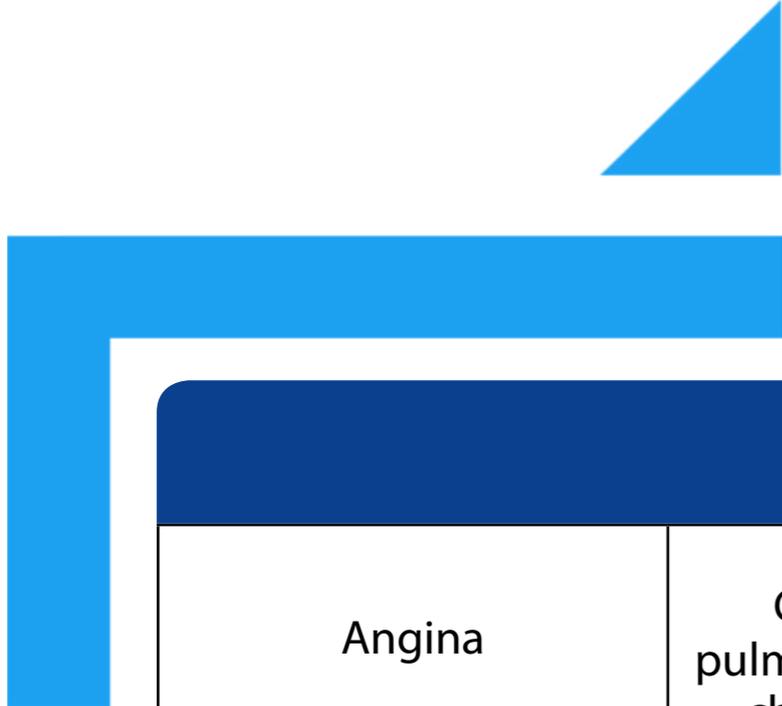
U.S. Department of Veterans Affairs

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Comorbid Conditions that Interfere with Sleep* [1, 2]

Medical			
Angina	Chronic obstructive pulmonary disease (COPD)/ chronic bronchitis and emphysema	Hyperthyroidism	Parkinson's disease
Arthritis	Epilepsy	Irritable bowel syndrome	Gastroesophageal reflux disease (GERD)
Asthma	Heart disease	Migraines	Restless legs syndrome
Pain	Hypertension	Nocturia	Sleep apnea

Psychiatric Disorders				
Anxiety disorders	Psychotic disorders	Depressive disorders	Substance use disorder	Posttraumatic Stress Disorder (PTSD)

*This is not an all-inclusive list.

Common Medications/Substances that Interfere with Sleep ^{[1, 3] [4]}

Category	Examples
Alcohol	Wine, beer, liquor
Antidepressants	Selective serotonin reuptake inhibitors (fluoxetine, sertraline, citalopram, escitalopram, fluvoxamine), venlafaxine, duloxetine, bupropion, monoamine oxidase inhibitors
Acetylcholinesterase inhibitors	Galantamine, donepezil, rivastigmine
Stimulants	Caffeine, methylphenidate, amphetamine derivatives, ephedrine and derivatives, cocaine
Decongestants	Pseudoephedrine, phenylephrine, phenylpropanolamine
Dopaminergic-related agents	Levodopa, pramipexole, ropinirole, tolcapone
Opioids and opioid antagonists	Oxycodone, codeine, hydrocodone Naltrexone
Cardiovascular agents	β -blockers, α -receptor agonists and antagonists, diuretics, lipid-lowering agents
Other	Albuterol, buspirone, corticosteroids, nicotine, theophylline

Sleep Guidance ^[5, 6]

1. Wake up at the same time every day regardless of the quality of your previous night's sleep.
2. Go to bed when you are sleepy, but not too early (for example, not before 10 p.m.). Long periods of time in bed will lead to shallow, broken sleep. You should spend only the amount of time in bed that you actually need for sleep. Sticking to the suggested bedtime/waketime will help you overcome your sleep problem.
3. Get up when you can't sleep. Go to another room until you feel sleepy enough to fall asleep quickly, then return to bed. Get up again if sleep does not come quickly.
4. Use the bed only for sleeping and sex. Do not read, eat, watch TV, etc., in bed.
5. Avoid napping in the late afternoon or early evening; it may interfere with your night's sleep.
6. Create a "buffer zone" or quiet time prior to bedtime. During this time, do things that are enjoyable on their own.
7. Don't worry, plan, etc., in bed. If you are worrying, planning, or can't shut off your thoughts, get up and stay up until you can return to bed without these mental activities interfering with your sleep.

Other Helpful Practices for Sleep Hygiene

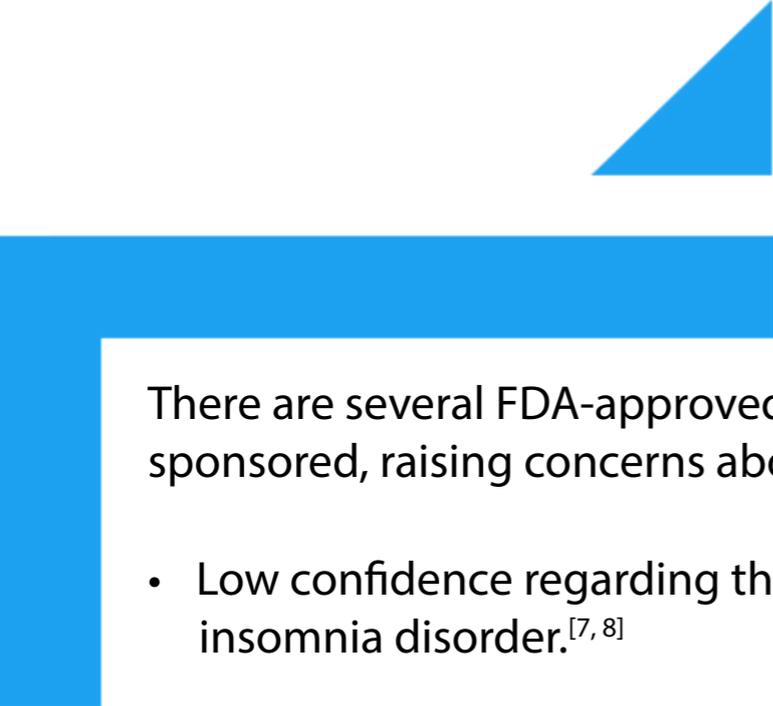
- Turn the clock away from you.
- Limit caffeine and consume it only before noon.
- Limit alcohol and do not consume it within three hours of bedtime.
- Exercise regularly, but not too close to bedtime.
- Keep the bedroom quiet, dark, and cool.
- Do not eat a heavy meal close to bedtime; a light bedtime snack such as milk, peanut butter, or cheese is OK.



Sleep Hygiene Education versus Cognitive Behavioral Therapy for Insomnia (CBT-I)^[6]

Sleep Hygiene Education	CBT-I
<ul style="list-style-type: none"> • Avoid stimulants for several hours before bedtime. • Avoid alcohol before bedtime. • Exercise regularly. • Allow at least a one-hour period to unwind before bedtime. • Keep the bedroom environment quiet, dark and comfortable. • Maintain a regular sleep schedule. 	<ul style="list-style-type: none"> • Sleep restriction • Stimulus control • Relaxation training • Cognitive behavioral therapy • Sleep hygiene education is covered during CBT-I
Standard guidelines	Individualized multi-component intervention
Helps normal sleepers maintain sleep health	Evidence-based treatment for insomnia disorder
Prevention	Treatment
Minimal impact on insomnia disorder	Very effective insomnia disorder treatment
Inactive condition in insomnia research	Active condition in insomnia research





Insomnia Disorder Pharmacotherapy

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.^[7, 8]
- 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.^[8]

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.

Recommended Dosages* [8-12]

Class	Agent	Usual Hypnotic Dose	Sedation Onset	Half-life	Guidance in Special Populations		
					Geriatric	Renal	Hepatic
Tricyclic antidepressants (TCAs)	Doxepin	3-6 mg	~30 min	~15 hrs	Initial: 3 mg Max: 5 mg	N/A	Max: 3 mg
	Amitriptyline	10-25 mg	Not specified	9-27 hrs	Use caution	N/A	Begin low, increase as tolerated
Anticonvulsant	Gabapentin	600-900 mg	Not specified	5-7 hr	N/A	Use caution if CrCl <60 ml/min	N/A
Antidepressant	Trazodone	25-100 mg	1-3 hrs	7-8 hrs	Use caution	N/A	N/A
	Mirtazapine	7.5-30 mg	Not specified	20-40 hrs	Bedtime dosing OK	Use caution if CrCl <40 ml/min	Titrate slowly
Antihistamine	Diphenhydramine	25-50 mg	1-3 hrs	2-10 hrs	N/A	Bedtime dosing OK	N/A
	Hydroxyzine	50-100 mg	15-30 min	~20 hrs	Initiate at low dose	↓by 50% if GFR >50ml/min	N/A
Melatonin Agonist	Ramelteon	8 mg	~30 min	1-3 hrs	N/A	N/A	Mild: Use caution; Severe: Not recommended

Recommended Dosages* [8-12]

Class	Agent	Usual Hypnotic Dose	Sedation Onset	Half-life	Guidance in Special Populations		
					Geriatric	Renal	Hepatic
Non-Benzodiazepine	Zolpidem IR	Women: 5 mg; Men: 5-10 mg	~30 min	2.5 hrs	Max: 5 mg Avoid use > 90 days	N/A	5 mg
	Zolpidem CR	Women: 6.25 mg; Men: 6.25 -12.5 mg	~30 min	2.8 hrs	Max: 6.25 mg Avoid use > 90 days	N/A	6.25 mg
	Eszopiclone	1-3 mg	Rapid (~10 mins)	6 hrs	2 mg	N/A	2 mg
	Zaleplon	5-10 mg	~30 min	~1 hr	Initial: 5 mg Max: 10 mg	N/A	Mild - Moderate: 5 mg; Severe: Not recommended
Orexin receptor antagonist	Suvorexant	10 mg daily	~30 min	12 hrs	N/A	N/A	Severe: Not studied

*This table is not a complete reference for prescribing these medications and provides general guidance only. Please see a drug information resource for complete prescribing information.

Contraindications and Precautions [8-10, 12]

Class	Agent	Contraindications	Precautions
TCA_s**	Doxepin	Narrow-angle glaucoma, severe urinary retention, monoamine oxidase inhibitor (MAOI) within 14 days, acute recovery phase of myocardial infraction (MI)	Risk of overdose: limit quantity for those at high risk of overdose
	Amitriptyline	Severe urinary retention, MAOI use within 14 days, acute recovery phase of MI	<ul style="list-style-type: none"> • Risk of conduction abnormalities • Not recommended with severe obstructive sleep apnea (OSA) • Risk of overdose: limit quantity for those at high risk of overdose • May↓ seizure threshold: avoid for those with a seizure disorder, head trauma, alcoholism
Anticonvulsant	Gabapentin	N/A	<ul style="list-style-type: none"> • Poor renal function • Risk of worsening mood/suicidal ideation** • ↓Bioavailability at higher doses
	Trazodone	Co-administration with an MAOI, including linezolid or IV methylene blue, use within 14 days of an MAOI	<ul style="list-style-type: none"> • Priapism • Caution in sickle cell anemia, multiple myeloma, leukemia • QT prolongation, serotonin syndrome

Contraindications and Precautions [8-10, 12]

Class	Agent	Contraindications	Precautions
Antidepressant**	Mirtazapine	MAOI use within 14 days	<ul style="list-style-type: none"> • Akathisia, blood dyscrasias (neutropenia/agranulocytosis) • May ↓ seizure threshold: avoid for those with a seizure disorder, head trauma, alcoholism
Antihistamine	Diphenhydramine Hydroxyzine	Acute asthma, breastfeeding, or early pregnancy	<ul style="list-style-type: none"> • Asthma, glaucoma, thyroid dysfunction • Cardiovascular disease* • Benign prostatic hyperplasia (BPH)/ urinary or pyloroduodenal obstruction • Cause sedation, use caution when performing tasks which require alertness (e.g., driving)
Melatonin Agonist	Ramelteon	History of angioedema with previous ramelteon therapy (do not rechallenge); concurrent fluvoxamine use	<ul style="list-style-type: none"> • Menses disruption, ↓ libido, respiratory depression • Hypersensitivity reactions

Contraindications and Precautions [8-10, 12]

Class	Agent	Contraindications	Precautions
Non-Benzodiazepine	Zolpidem Eszopiclone Zaleplon	Zolpidem: Canadian labeling: Significant OSA and acute or severe respiratory impairment; myasthenia gravis; severe hepatic impairment; personal or family history of sleepwalking	<ul style="list-style-type: none"> • Anaphylaxis or angioedema with first or subsequent doses • Central nervous system (CNS) impairment may not be reliably detected by routine exam; risk increases in the debilitated and elderly, patients with less than a full night's sleep (7-8 hrs), higher doses, and use of other CNS depressants • Abnormal thinking/behavior changes • Complex sleep-related activities • The failure of insomnia to remit after –seven to 10 days of treatment may indicate the presence of a primary psychiatric and/ or medical illness
Orexin receptor antagonist	Suvorexant	Patients with narcolepsy	<ul style="list-style-type: none"> • Daytime somnolence, nighttime “sleep-driving”; risk increases with dose, with use of CNS depressants/alcohol • Depression: Worsening of depression or suicidal thinking • Compromised respiratory function • Sleep paralysis, hypnagogic/hypnopompic hallucinations, and cataplexy-like symptoms

Disclaimer: This is a quick reference guide. For complete prescribing information, please see package insert.

*Cardiovascular Disease = Previous MI, stroke, tachycardia, or conductive abnormalities;

**Monitor for worsening of mood or suicidal ideation when starting anticonvulsants and antidepressants.



Insomnia Disorder - Quick Reference Guide

This reference guide was created as a tool for VA providers and is available from the Academic Detailing SharePoint.

VA PBM Academic Detailing Service Email Group: PharmacyAcademicDetailingProgram@va.gov

VA PBM Academic Detailing Service SharePoint Site: <https://vaww.portal2.va.gov/sites/ad>

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