

Table. Medications used to treat insomnia

Medication	Mechanism of action	FDA approved for insomnia?	Dose (mg)	Use in pregnancy and lactation	Precautions	Recommended by AASM?	Beers Criteria	Comments
Nonprescription medications								
Melatonin, a hormone produced endogenously by the pineal glands ^{a,e}	Regulation of the sleep–wake cycle through its actions on melatonin receptors in the suprachiasmatic nucleus	Not categorized as a drug Used for sleep onset and sleep maintenance, but only weak evidence to support efficacy	0.2-5.0*	Should not be used during pregnancy or lactation without further studies	Because it inhibits CYP1A2 substrates, it may increase concentrations of drugs such as fluvoxamine, an SSRI, and warfarin, an anticoagulant.	No for sleep onset, no for sleep maintenance	—	Can cause tachycardia, flushing, itching, headaches, and vivid dreams. Should not be administered with a high-fat meal, which reduces absorption.
Valerian root, an herbal product ^{a,e-h}	Modulation of GABA-ergic transmission	Not categorized as a drug Used for sleep onset and sleep maintenance, but no evidence to support efficacy	300-600*	Should not be used during pregnancy or lactation without further studies	Interacts adversely with general anesthetics; must be stopped ≥1 week before surgery. Long-time users can experience BZ-like withdrawal symptoms. Should not be used in persons with liver or pancreatic disease.	No for sleep onset, no for sleep maintenance	—	Used to treat anxiety as well as insomnia. Can cause headache, stomach upset, mental dullness, excitability, heart disturbances, and even insomnia.
Diphenhydramine, used primarily as an antihistamine ^{a,e,i-k}	Histamine H1 antagonist	Yes Used for sleep onset and sleep maintenance; no strong evidence to support efficacy	12.5-50*	May be used in pregnancy, but not by lactating mothers; can lead to CNS depression in infant and may decrease breast milk production	Should be avoided by persons older than 65 years, primarily because of its sedative and anticholinergic effects	No for sleep onset, no for sleep maintenance	Avoid	Can cause constipation, dry mouth, difficulty urinating, upset stomach, blurred vision, tremor, loss of appetite, headache
Benzodiazepine hypnotics (Schedule IV drugs)								
Temazepam (Restoril) ^{e,k,m}	See article text on class description	Yes Indicated for sleep onset and sleep maintenance	7.5-30	Pregnancy Category X; should be used with caution by nursing mothers	Should be used with caution in persons with respiratory depression or chronic obstructive pulmonary disease, in those with impaired renal or hepatic function, and in older adults.	Yes for both sleep onset and sleep maintenance	Avoid	Because the drug has no active metabolite, cognitive impairment and grogginess the following day are reduced.
Triazolam (Halcion) ^{e,k,l,n}	See article text on class description	Yes Indicated for sleep onset	0.125-0.5	Pregnancy Category X; should not be used by nursing mothers	Should not be used with drugs that significantly impair the oxidative metabolism mediated by CYP3A (e.g., ketoconazole, itraconazole, nefazodone, several HIV protease inhibitors). Dosing should be adjusted in patients with hepatic impairment.	Yes for sleep onset	Avoid	
Nonbenzodiazepine hypnotics (Schedule IV drugs)								
Eszopiclone (Lunesta) ^{e,k,o}	See article text on class description	Yes Indicated for sleep onset and sleep maintenance	1-3	Data are insufficient to make definitive recommendations	In patients with severe hepatic impairment or in those taking other potent CYP3A4 inhibitors (e.g., ketoconazole, clarithromycin, ritonavir), the dose should not exceed 2 mg.	Yes for both sleep onset and sleep maintenance	Avoid	
Zaleplon (Sonata) ^{e,k,p}	See article text on class description	Yes Indicated for sleep onset	5-20†	Pregnancy Category C; can be used with caution by nursing mothers	See article text on class description	Yes for sleep onset	Avoid	
Zolpidem (Ambien, Ambien CR) ^{a,k,q,r}	See article text on class description	Yes Indicated for sleep onset (Ambien) or sleep onset and sleep maintenance (Ambien CR)	5-10; 6.25-12.5	Pregnancy Category C; can be used with caution by nursing mothers	See article text on class description	Yes for both sleep onset and sleep maintenance	Avoid	

Miscellaneous hypnotics								
Ramelteon (Rozerem), a melatonin agonist ^{e,k,s}	Melatonin receptor agonist with both high affinity for melatonin MT1 and MT2 receptors and relative selectivity over the MT3 receptor	Yes Indicated for sleep onset	8	Pregnancy Category C; can be used with caution by nursing mothers	Should not be used in patients with severe hepatic impairment or with the SSRI fluvoxamine, and should be used with caution in patients with moderate hepatic impairment and in those taking other CYP1A2-inhibiting drugs. Avoid in patients with severe sleep apnea.	Yes for sleep onset	Can be used in older adults	Should not be administered with a high-fat meal, which reduces absorption
Trazodone (Desyrel), an antidepressant ^{e,k,t,u}	Not fully understood; thought to enhance serotonergic activity in the CNS	No, but used off label, often as an adjunct to SSRI treatment	25-150*	Pregnancy Category C; can be used with caution in nursing mothers	Can cause excessive sedation and anticholinergic effects, prolong QT interval, cause OH and syncope, increase risk of bleeding when used with anticoagulants or antiplatelet drugs, and aggravate glaucoma	No for sleep onset, no for sleep maintenance	Can be used with caution in older adults	As with all antidepressants, PI has boxed warning regarding risk for suicidality in pediatric and young adult patients
Doxepin (Silenor), a TCA prescribed in a very low dose ^{e,k,v}	Central histamine H1 receptor antagonist	Yes Indicated for sleep maintenance	3-6	Pregnancy Category C; may be harmful to infants of lactating mothers	Contraindicated in patients with glaucoma or severe urinary retention. Users should avoid eating within 3 hours of taking the medication.	Yes for sleep maintenance	Can be used with caution in older adults	See above about boxed warning
Mirtazapine (Remeron), a tetracyclic antidepressant ^{e,k,w}	Serotonin receptor and histamine receptor antagonist	No, but used off label to treat insomnia	15-45*	Pregnancy Category C drug; can be used with caution by nursing mothers	For patients wishing to stop long-term treatment, the drug should be tapered gradually, not stopped abruptly, to avoid withdrawal symptoms. See PI for multiple precautions.	Not mentioned	Can be used with caution in older adults	See above about boxed warning; may be helpful for patients who need to gain weight
Suvorexant (Belsomra), an orexin inhibitor agonist ^{e,k,x}	Highly selective antagonist of orexin receptors (turns off wakefulness centers)	Yes Indicated for sleep onset and sleep maintenance	5-20	Pregnancy Category C; can be used with caution in nursing mothers	Schedule IV drug. Can cause complex sleep behaviors. Should be taken only if patient can get a full night's sleep. Dose should be 5 mg when used with moderate CYP3A inhibitors. Can be raised to 10 mg if 5 mg not effective. Avoid in patients using strong CYP3A inhibitors.	Yes for sleep maintenance	Can be used in older adults	Time to effect may be delayed if taken with or soon after a meal

*Suggested dose or dose range. These agents are not FDA approved to treat insomnia. †Maximum dose in older adults, 10 mg. AASM, American Academy of Sleep Medicine; BZ, benzodiazepine; CNS, central nervous system; OH, orthostatic hypotension; PI, prescribing information; SSRI, selective serotonin reuptake inhibitor; TCA, tricyclic antidepressant.

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