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Insomnia-Causing Medications: A Clinical Reference Guide

Sleep disturbances affect most people at some stage in their lives and this is a common reason for primary care consultations. Widely understood factors that impact sleep include sleep hygiene, proximity of exercise/meals to bedtime, use of digital devices, and alcohol consumption. However, perhaps less often considered is the association between medicines and disturbed sleep, e.g. beta blockers. When prescribing medicines to treat one condition, it can sometimes be difficult to weigh this up against the unintended consequences for another aspect of the patient's wellbeing.

Key considerations

Clinicians should consider the variable impacts of medications on sleep when prescribing, especially for patients with existing sleep problems.' Antidepressants are well known to affect sleep, however, there is variation in the adverse effect profiles of individual medicines which complicates prescribing, e.g. bupropion can cause insomnia whereas mirtazapine may cause sedation. In contrast, diuretics may improve sleep for patients with obstructive sleep apnoea (by reducing fluid retention), but this must be balanced against nocturia causing possible sleep disruption.

COMPOUNDING FACTORS

Polypharmacy where there is concurrent use of multiple medications amplifying insomnia related side effects contributes to worsening sleep disorders." Efforts to reduce polypharmacy and improve prescribing practices could alleviate these side effects and enhance population health.

Top 50 Medications causing Insomnia		
MEDICATIONS	**Class of medicine**	**Insomnia Risk (mild to high)**
Bupropion	NDRI Antidepressant	High
Methylphenidate	CNS Stimulant	High
Dextroamphetamine / Amphetamine	CNS Stimulant	High
Lisdexamfetamine	CNS Stimulant	High
Modafinil	Wakefulness Agent	High
Armodafinil	Wakefulness Agent	High
Fluoxetine	SSRI	High
Sertraline	SSRI	High
Venlafaxine	SNRI	High
Duloxetine	SNRI	High
Phenelzine	MAOI	High
Selegiline	MAOI	High
Theophylline	Bronchodilator	High
Pseudoephedrine	Decongestant	High
Dexamethasone	Glucocorticoid	High
Prednisone	Glucocorticoid	High
Hydrocortisone	Corticosteroid	High
Atomoxetine	NRI	High
Nicotine	Stimulant / Smoking Cessation	High
Levodopa / Carbidopa	Dopaminergic Agent	Moderate–High
Metoprolol	Beta-Blocker	Moderate–High
Paroxetine	SSRI	Moderate

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MEDICATIONS	Class of medicine	Insomnia Risk (mild to high)
Citalopram	SSRI	Moderate
Escitalopram	SSRI	Moderate
Desvenlafaxine	Desvenlafaxine	Moderate
Pramipexole	Dopamine Agonist	Moderate
Ropinirole	Dopamine Agonist	Moderate
Varenicline	Smoking Cessation Agent	Moderate
Propranolol	Beta-Blocker	Moderate
Clonidine	Alpha-2 Agonist	Moderate
Guanfacine	Alpha-2 Agonist	Moderate
Levofloxacin	Antibiotic	Moderate
Ciprofloxacin	Antibiotic	Moderate
Lamotrigine	Anticonvulsant	Moderate
Atenolol	Beta-Blocker	Moderate
Oxybutynin	Anticholinergic / Bladder Agent	Moderate
Phenytoin	Anticonvulsant	Moderate
Topiramate	Anticonvulsant	Moderate
Tamsulosin	Alpha-Blocker	Low–Moderate
Doxazosin	Alpha-Blocker	Low–Moderate
Montelukast	Leukotriene Receptor Antagonist	Low–Moderate
Albuterol	Beta-2 Agonist	Low–Moderate
Diphenhydramine	Antihistamine	Low (rebound High)
Codeine	Opioid Analgesic	Low–Moderate (rebound risk)
Levothyroxine	Thyroid Hormone	Low
Simvastatin	Statin	Low
Atorvastatin	Statin	Low
Omeprazole	Proton Pump Inhibitor	Low-High*
Esomeprazole	Proton Pump Inhibitor	Low-High*
Ranitidine	H2 Receptor Antagonist	Low

- Proton Pump Inhibitors can help with reflux related sleep issues so are generally regarded as having a lower risk of causing insomnia however because they cause hypomagnesemia they can have a detrimental effect on sleep over time.

' Klugherz LJ, Mansukhani MP, Kolla BP. Effects of Commonly Prescribed Medications on Sleep: A Review of the Literature. Mayo Clin Proc. 2025;100(5):856-867. doi:10.1016/j.mayocp.2025.02.005
" Do D. Trends in the use of medications with insomnia side effects and the implications for insomnia among US adults. J Sleep Res. 2020;29:e13075. https://doi.org/10.1111/jsr.1307513652869, 2020, 4.