ALPHA-1 ADRENERGIC ANTAGONIST

Prazosin

Minipress

Antihypertensive alpha-1 blocker used off-label at bedtime for PTSD trauma nightmares and sleep disruption.

NIGHTMARE DOSE RANGE	HALF-LIFE	METABOLISM	ONSET
2-15 mg PO at bedtime	**2-3 h; BP effect 6-10 h**	**Hepatic; biliary excretion**	**Nightmares improve in 1-2 wks**

No FDA boxed warning on the current US label.

INDICATIONS

- FDA-approved only for hypertension in adults; every psychiatric use of prazosin described below is off-label.
- Used off-label for PTSD-related nightmares and sleep disruption, the best-studied psychiatric application of the drug.
- The American Academy of Sleep Medicine position paper states prazosin may be used for PTSD-associated nightmares, a conditional recommendation.
- Trial results conflict: earlier studies in active-duty soldiers were positive while the 2018 multicenter veteran trial found no benefit over placebo.
- Used off-label for daytime PTSD hyperarousal with a small added morning or afternoon dose in patients who respond at night.
- Occasionally used off-label for alcohol use disorder craving and for benign prostatic hyperplasia symptoms, where other alpha blockers are preferred.

DOSING & TITRATION

- PTSD nightmares off-label: start **1 mg** PO at bedtime, warning the patient about first-dose hypotension and syncope.
- Increase every 3 to 7 days as tolerated through 2, 4, 6, and 10 mg; typical effective doses are **6-15 mg** at bedtime in men.
- Women often respond at lower doses, with mean effective doses near **7-10 mg** compared with about **13-15 mg** in men.
- For daytime hyperarousal, add **1-2 mg** in the morning or afternoon only after the bedtime dose is established and tolerated.
- Hypertension labeling: **1 mg** two or three times daily, increased slowly, with usual maintenance doses of 6-15 mg/day divided.
- Taper rather than stop abruptly after prolonged higher doses, and restart at 1 mg if a patient has missed several days.

MECHANISM OF ACTION

- Selectively blocks postsynaptic alpha-1 adrenergic receptors, causing arterial and venous dilation and lowering blood pressure.
- It is lipophilic and crosses the blood-brain barrier, unlike some peripheral alpha-1 blockers, which allows a central effect on sleep.
- Central alpha-1 blockade is thought to dampen noradrenergic activity during rapid eye movement sleep, reducing nightmare intensity.
- Prazosin does not sedate directly; improved sleep continuity comes from suppressing nocturnal noradrenergic surges rather than hypnosis.
- Peripheral alpha-1 blockade also relaxes bladder neck and prostatic smooth muscle, explaining urinary effects and the floppy iris syndrome.

PHARMACOKINETICS

- Tmax is 1-3 hours after oral dosing, so bedtime dosing places the peak effect during the first half of the sleep period.
- Elimination half-life is 2-3 hours, while the antihypertensive effect lasts 6-10 hours, which supports a second daytime dose if needed.
- Extensively metabolized in the liver by demethylation and conjugation, with excretion mainly in bile and feces rather than urine.
- Protein binding is high at about 97 percent, and bioavailability ranges widely between 43 and 82 percent across individuals.
- The short half-life means nightmares typically return within a night or two of stopping, which patients should be told in advance.

ADVERSE EFFECTS

- Dizziness in about 10 percent, headache, drowsiness, fatigue, and palpitations are the most common effects at initiation.
- First-dose phenomenon of marked orthostatic hypotension and syncope occurs within 30 to 90 minutes, which is why the first dose is at bedtime.
- Nasal congestion, dry mouth, and urinary frequency are common and occasionally lead to discontinuation despite benefit for nightmares.
- Priapism is rare but requires emergency urologic care, and patients should be told explicitly to seek help for prolonged erection.
- Intraoperative floppy iris syndrome can complicate cataract surgery, so any ophthalmologist should be told the patient takes prazosin.
- Rebound nightmares or sleep disruption occur within one or two nights of stopping because of the short half-life.

MONITORING

- Check blood pressure and orthostatic vitals at baseline, after the first dose is established, and after each titration step.
- Ask directly about dizziness on standing, near-syncope, and falls, particularly in older adults and patients on other antihypertensives.
- Track nightmare frequency and intensity with a nightmare diary or the CAPS-5 recurrent distressing dreams item rather than global impressions.
- Reassess dose adequacy at 4 weeks, since undertreatment at 1-2 mg is the most common reason prazosin appears to fail.
- Screen for daytime hyperarousal separately, since bedtime-only dosing leaves daytime symptoms untreated.

INTERACTIONS & CAUTIONS

- Additive hypotension with other antihypertensives, nitrates, and particularly with phosphodiesterase-5 inhibitors such as sildenafil and tadalafil.
- Beta-blockers and calcium channel blockers increase the risk and severity of the first-dose orthostatic reaction.
- Alcohol and other sedatives worsen orthostatic symptoms and increase fall risk when taken near the bedtime dose.
- Nonsteroidal anti-inflammatory drugs and sympathomimetics blunt the antihypertensive effect and can reduce clinical benefit.
- No significant CYP-mediated interactions are established, which makes prazosin easy to combine with most psychotropic regimens.

SPECIAL POPULATIONS

- Pregnancy: limited human data; prazosin has been used for hypertension and pheochromocytoma in pregnancy when clearly needed.
- Lactation: small amounts appear in human milk, so monitor the infant for sedation and poor feeding if breastfeeding continues.
- Pediatric: safety and effectiveness are not established, though small studies describe use for pediatric PTSD nightmares off-label.
- Geriatric: begin at 1 mg, titrate slowly, and weigh fall and fracture risk against nightmare relief in frail patients.
- Renal impairment: no formal adjustment is required, but patients with severe impairment often respond to lower doses.

PRESCRIBING PEARLS

- First dose is always 1 mg at bedtime; the first-dose syncope reaction is real and preventable.
- Most prazosin failures are underdosing; men often need 10-15 mg at night to stop nightmares.
- Warn about floppy iris syndrome before cataract surgery and priapism as an emergency.

References

MedlinePlus. (2024). *Prazosin*. U.S. National Library of Medicine. https://medlineplus.gov/druginfo/meds/a682245.html

Morgenthaler, T. I., Auerbach, S., Casey, K. R., Kristo, D., Maganti, R., Ramar, K., Zak, R., & Kartje, R. (2018). Position paper for the treatment of nightmare disorder in adults: An American Academy of Sleep Medicine position paper. *Journal of Clinical Sleep Medicine, 14*(6), 1041-1055. https://doi.org/10.5664/jcsm.7178

National Institute of Diabetes and Digestive and Kidney Diseases. (2020). Prazosin. In *LiverTox: Clinical and research information on drug-induced liver injury*. https://www.ncbi.nlm.nih.gov/books/NBK548699/

Pfizer. (2023). *Minipress (prazosin hydrochloride) capsules [Prescribing information]*. U.S. Food and Drug Administration. https://dailymed.nlm.nih.gov/dailymed/

Raskind, M. A., Peskind, E. R., Chow, B., Harris, C., Davis-Karim, A., Holmes, H. A., Hart, K. L., McFall, M., Mellman, T. A., Reist, C., Romesser, J., Rosenheck, R., Shih, M. C., Stein, M. B., Swift, R., Gleason, T., Lu, Y., & Huang, G. D. (2018). Trial of prazosin for post-traumatic stress disorder in military veterans. *New England Journal of Medicine, 378*(6), 507-517. https://doi.org/10.1056/NEJMoa1507598

Stahl, S. M. (2021). *Stahl's essential psychopharmacology: Neuroscientific basis and practical applications* (5th ed.). Cambridge University Press.

Yucel, D. E., van Emmerik, A. A. P., Souama, C., & Lancee, J. (2020). Comparative efficacy of imagery rehearsal therapy and prazosin in the treatment of trauma-related nightmares in adults: A meta-analysis of randomized controlled trials. *Sleep Medicine Reviews, 50*, 101248. https://doi.org/10.1016/j.smrv.2019.101248

NOTE

References follow APA 7th edition style. Dosing, boxed warnings, and interaction data change; confirm every clinical decision against the current FDA prescribing information (DailyMed) and your institution's formulary. This sheet is an educational quick reference and does not replace the full label or clinical judgment.