

Q. What is prazosin?

A. Prazosin is a noradrenaline alpha-blocker medication with Food and Drug Administration (FDA) approval for the treatment of hypertension to lower blood pressure (U.S. Food and Drug Administration, 2009). Prazosin is used off-label to treat anxiety, posttraumatic stress disorder (PTSD), and trauma-related nightmares.

Q. What are the potential mechanisms of action underlying prazosin?

A. Dysregulation of the adrenergic system was first identified as a contributing mechanism in PTSD decades ago (Kosten, Mason, Giller, Ostroff, & Harkness, 1987), and it is hypothesized that dysregulation of noradrenergic neurons is specifically associated with hyperarousal and re-experiencing symptoms (Southwick et al., 1997). Prazosin, an α_1 -adrenergic receptor antagonist, is thought to counteract the noradrenergic hyperactivity that results in the intrusive and hyperarousal symptoms characteristic of PTSD. Similarly, α_1 -adrenergic receptor stimulation is thought to contribute to sleep disruption and trauma nightmares (Boehnlein & Kinzie, 2007; Mellman, Kumar, Kulick-Bell, Kumar, & Nolan, 1995).

Q. Is prazosin recommended as a front-line treatment for PTSD/trauma-related nightmares in the Military Health System (MHS)?

A. **No.** The 2017 VA/DoD Clinical Practice Guideline (CPG) for the Management of Posttraumatic Stress Disorder and Acute Stress Disorder gives a “Weak Against” strength of recommendation for prazosin to treat global symptoms of PTSD, either as a monotherapy or augmentation therapy. In addition, the CPG states that there is insufficient evidence to recommend for or against the use of prazosin as a monotherapy or augmentation therapy for nightmares associated with PTSD.

The MHS relies on the VA/DoD CPGs to inform best clinical practices. The CPGs are developed under the purview of clinical experts and are derived through a transparent and systematic approach that includes, but is not limited to, systematic reviews of the literature on a given topic and development of recommendations using a graded system that takes into account the overall quality of the evidence and the magnitude of the net benefit of the recommendation. A further description of this process and CPGs on specific topics can be found on the VA clinical practice guidelines website.

Q. Do other authoritative reviews recommend prazosin as a front-line treatment for PTSD/trauma-related nightmares?

A. **No.** Other authoritative reviews have not substantiated the use of prazosin for PTSD/trauma-related nightmares.

Several other recognized organizations conduct systematic reviews and evidence syntheses on psychological health topics using similar grading systems as the VA/DoD CPGs. These include the Agency for Healthcare Research and Quality (AHRQ) and Cochrane.

- AHRQ: A 2018 systematic review update of psychological and pharmacological treatments for adults with PTSD found that prazosin reduced PTSD symptoms, but the strength of evidence was low (Forman-Hoffman et al., 2018).
- Cochrane: No systematic reviews evaluating prazosin as a treatment for PTSD/trauma-related nightmares were identified.

Q. Is there any recent research on prazosin as a treatment for PTSD/trauma-related nightmares?

A. A June 2018 literature search identified two randomized controlled trials (RCTs) published after the earlier literature search was conducted for the 2017 VA/DoD Clinical Practice Guideline for the Management of Posttraumatic Stress Disorder and Acute Stress Disorder. The first RCT was conducted with 32 veterans with war-related PTSD who were randomly assigned to receive prazosin or a placebo for eight weeks (Khazaie, Nasouri, & Ghadami, 2016). There were no significant differences found between treatment

groups on PTSD symptoms or trauma-related nightmares. Although published in 2018, results from the second RCT were evaluated and taken into consideration for the *2017 VA/DoD Clinical Practice Guideline for the Management of Posttraumatic Stress Disorder and Acute Stress Disorder* (Raskind et al., 2018).

Q. What conclusions can be drawn about the use of prazosin as a treatment for PTSD/trauma-related nightmares in the MHS?

A. Although results from early RCTs evaluating prazosin as a treatment for PTSD/trauma-related nightmares appeared promising (Germain et al., 2012; Raskind et al., 2003; Raskind et al., 2007; Raskind et al., 2013), these trials varied in quality, and a more recent, large, well-designed trial did not find prazosin to be efficacious for either PTSD symptoms or nightmares (Raskind et al., 2018). Thus, prazosin is not recommended as a front-line treatment for PTSD or trauma-related nightmares in the MHS.

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