Venlafaxine for Posttraumatic Stress Disorder

Q. What is venlafaxine?

A. Venlafaxine is a generic drug belonging to a class known as dual serotonin and norepinephrine reuptake inhibitors (SNRIs). Brand names include Effexor and Effexor XR (extended release). Venlafaxine is most commonly prescribed in oral pill form as an antidepressant. It also is regularly prescribed for posttraumatic stress disorder (PTSD) and premenstrual dysphoric disorder, and is approved by the U.S. Food and Drug Administration (FDA) for the treatment of depression, generalized anxiety disorder, social anxiety disorder, and panic disorder. Venlafaxine may be effective in patients who fail to respond to selective serotonin reuptake inhibitors (SSRIs) and may be used in combination with other antidepressants for treatment-refractory cases (Stahl, 2017).

Q. What are the potential mechanisms of action underlying venlafaxine for the treatment of PTSD?

A. It has been suggested that noradrenergic dysregulation plays a significant role in the development and maintenance of PTSD symptoms. Conditioned fear responses can produce chronic hyperarousal and re-experiencing of symptoms, which in turn may lead to avoidance behaviors and emotional numbing. Conditioned fear responses are linked to norepinephrine dysregulating nerves from the locus coeruleus to the amygdala, prefrontal cortex, and hippocampus (Charney, Deutsch, Krystal, Southwick, & Davis, 1993). Serotonin either directly or indirectly regulates activity of norepinephrine (Newport and Nemeroff, 2000). Venlafaxine XR may reduce hyperarousal and re-experiencing core symptoms of PTSD by blocking reuptake of both norepinephrine and serotonin (Stein et al., 2003).

Q. Is venlafaxine recommended as a treatment for PTSD in the Military Health System (MHS)?

A. **Yes.** The *2017 VA/DoD Clinical Practice Guideline for the Management of Posttraumatic Stress Disorder and Acute Stress Disorder* recommends venlafaxine as monotherapy for patients diagnosed with PTSD who choose not to engage in or are unable to access trauma-focused psychotherapy, with a "strong for" strength of recommendation.

The MHS relies on the VA/DoD clinical practice guidelines (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 venlafaxine as a treatment for PTSD?

A. **Yes.** Other authoritative reviews have substantiated the use of venlafaxine for PTSD.

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 venlafaxine reduced PTSD symptoms and was associated with greater PTSD symptom remission, with a moderate strength of evidence (Forman-Hoffman et al., 2018). However, among pharmacological treatments with at least moderate strength of evidence of benefit, venlafaxine also was associated with nausea, the only adverse event with at least a moderate strength of evidence.
- Cochrane: No systematic reviews on venlafaxine for PTSD were identified.

Q. What conclusions can be drawn about the use of venlafaxine as a treatment for PTSD in the MHS?

A. The *2017 VA/DoD Clinical Practice Guideline for the Management of Posttraumatic Stress Disorder and Acute Stress Disorder* recommends venlafaxine as monotherapy for PTSD for patients diagnosed with PTSD who choose not to engage in or are unable to access trauma-focused psychotherapy. The CPG recommends individual, manualized trauma-focused psychotherapy over pharmacologic interventions for the primary treatment of PTSD. Clinicians should consider several factors when choosing a treatment with their patient. Treatment decisions should take into account practical considerations such as availability and patient preference that might influence treatment engagement and retention.

References

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