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Q: What is naltrexone?

A: Naltrexone is a medication used originally for opioid addiction that is approved by the U.S. Food and Drug Administration (FDA) for the treatment of alcohol use disorder (AUD). Naltrexone is administered either in a once-daily oral formulation or by an extended-release monthly injection. The long-acting, injectable formulation may be preferred when medication adherence is a concern but must be refrigerated and administered by a provider.

Q: What are the potential mechanisms of action underlying naltrexone?

A: The mechanism of action underlying naltrexone as a treatment for AUD is not fully understood. The stimulating and reinforcing effects of alcohol involve several neurotransmitter systems, but research has focused on the central role of mesolimbic dopamine (Ray, Chin, & Miotto, 2010). Alcohol use induces release of endogenous opioids, leading to opioid receptor activation and increased dopamine release in the nucleus accumbens. Naltrexone is an opioid receptor antagonist and reduces the release of dopamine resulting from alcohol use, suppressing its rewarding effects. In line with these pharmacological effects, human laboratory studies have found that naltrexone reduces craving and alcohol self-administration (Hendershot, Wardell, Samokhvalov, & Rehm, 2016).

Q: Is naltrexone recommended as a treatment for AUD in the Military Health System (MHS)?

A: Yes. The 2021 VA/DoD Clinical Practice Guideline for the Management of Substance Use Disorders gives a “strong for” strength of recommendation to naltrexone (both oral and extended release) for patients with moderate to severe alcohol use disorder.

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 naltrexone as a treatment for AUD?

A: Yes. Other authoritative reviews and guidelines have substantiated the use of naltrexone as a treatment for AUD.

Other recognized organizations conduct systematic reviews and evidence syntheses on psychological health topics using similar grading systems as the VA/DoD CPGs. Most notable of these organizations is Cochrane – an international network that conducts high-quality reviews of healthcare interventions.

- Cochrane: A 2014 systematic review reported that naltrexone was comparable to anticonvulsants in affecting severe relapse and continuous abstinence rates, though evidence was limited (Pani et al., 2014).

Q: What conclusions can be drawn about the use of naltrexone as a treatment for AUD in the MHS?

A: Along with topiramate (an anticonvulsant), naltrexone is considered a front-line pharmacological treatment for AUD. The CPG states that there is insufficient evidence to recommend one of these medications over another, and that these medications should be used in conjunction with a psychosocial intervention. Providers should consider factors such as potential adverse effects, comorbidities, and availability when selecting a treatment with patients.

References

Department of Veterans Affairs/Department of Defense. (2015). *VA/DoD clinical practice guideline for the management of substance use disorders. Version 3.0*. Washington, DC: Department of Veterans Affairs/Department of Defense.

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