Topiramate for Alcohol Use Disorder

Psychological Health Center of Excellence Psych Health Evidence Briefs April 2018

Q. What is topiramate?

A. Topiramate is an anticonvulsant medication most commonly prescribed for epilepsy and migraine headaches. Topiramate is not approved by the U.S. Food and Drug Administration (FDA) for the treatment of alcohol use disorder (AUD), although off-label use for the treatment of AUD has increased in recent years. As topiramate is "off-patent," it is unlikely to go through the FDA approval process to become an FDA-approved treatment for AUD (Blodgett, Del Re, Maisel, & Finney, 2014).

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

A. It is hypothesized that topiramate decreases alcohol reinforcement by reducing dopamine release, specifically via facilitation of gamma-aminobutyric acid (GABA) activity and inhibition of glutamate activity on specific receptors (Johnson et al., 2007).

Q. Is topiramate recommended as a front-line treatment for AUD in the Military Health System (MHS)?

A. Yes. The 2015 VA/DoD Clinical Practice Guideline for the Management of Substance Use Disorders gives a "strong for" strength of recommendation to topiramate for patients with moderate-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 topiramate as a front-line treatment for AUD?

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

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), the American Psychiatric Association (APA), and Cochrane.

- AHRQ: A 2014 AHRQ comparative effectiveness review of pharmacotherapy for adults with AUD in the outpatient setting found moderate evidence supporting the efficacy of topiramate for improving some consumption outcomes, including reduced drinking days, heavy drinking days, and drinks per drinking day (Jonas et al., 2014).
- APA: The APA Practice Guideline for the Pharmacological Treatment of Patients with Alcohol Use Disorder recommends "topiramate or gabapentin be offered to patients with moderate to severe alcohol use disorder who: 1) have a goal of reducing alcohol consumption or achieving abstinence, 2) prefer topiramate or gabapentin or are intolerant to or have not responded to naltrexone and acamprosate, and 3) have no contraindications to the use of these medications" (APA, 2018).
- Cochrane: A 2014 systematic review (Pani, Trogu, Pacini, & Maremmani) on anticonvulsants, primarily topiramate, for alcohol dependence found that anticonvulsants were more effective than placebo for certain outcomes, including number of drinks per drinking day and average heavy drinking. However, due to the high degree of heterogeneity, and the low number and quality of the studies comparing anticonvulsants to other medications, the authors conclude that there is "insufficient" randomized evidence supporting the use of anticonvulsants to treat alcohol dependence.

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

A. Along with naltrexone and acamprosate, topiramate has met the burden of evidence for inclusion in VA/DoD guidelines and is considered a front line pharmacological treatment for AUD. Topiramate is associated with certain side effects to include numbness, anorexia, taste abnormalities, cognitive impairment, and rash. Providers should take into account factors such as potential adverse effects, comorbidities, and availability to inform treatment choice for patients with AUD.

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Released April 2018 by the Psychological Health Center of Excellence.
This product is reviewed annually and is current until superseded.
301-295-7681 | pdhealth.mil PUID 4835