Other Pharmacotherapy Options for AUD

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While the following medications are all interesting treatment options, some novel, and others repurposed therapeutics, further research is necessary. At this time, they ***should not be prescribed in the ED for AUD***.

GLP-1 Agonists: These medications are thought to work in various substance use disorders, by their downstream effects, and modulation of dopamine in the reward regions of the brain.[30] Medications such as semaglutide and liraglutide are actively being investigated for their use in AUD. In one RCT, semaglutide, initiated at a dose of 0.25 mg weekly, was found to significantly reduce cravings and the number of drinks.[31] Another retrospective study comparing both semaglutide and liraglutide demonstrated that they were associated with a 30 to 40 percent reduced risk of hospitalizations due to AUD compared to other forms of MAUD.[32]

Prazosin: Another area of research is to determine which medications can be used in conjunction with commonly prescribed forms of MAUD to improve efficacy. Prazosin, an alpha-1 antagonist, is an FDA-approved medication for hypertension and used off-label for post-traumatic stress disorder. In a study of 31 veterans with AUD, it was shown that groups taking prazosin and naltrexone had more than 50 percent reductions in alcohol consumption metrics compared to control groups.[33]

Baclofen: A muscle relaxant and GABA-B agonist, baclofen was recently approved for the management of AUD in France.[34] It has been utilized, off-label, for the management of AUD, due to its GABA-B agonism, but there is wide variability in dosing regimens, and studies have been inconclusive when compared to other agents. One recent meta-analysis found that when compared to placebo groups, baclofen was not superior in decreasing heavy drinking days or cravings.[35] More recent studies, have found that baclofen may be effective, but likely requires tailoring doses to specific patients, further increasing the difficulty in its widespread use.[36]

Varenicline: A nicotinic acetylcholine receptor agonist that is effective in smoking cessation has also been a medication garnering interest as a potential treatment option for AUD. Studies on its use have yielded mixed results. A recently published meta-analysis investigating varenicline use for patients with alcohol dependence found that in 21 RCTs there were varying outcomes. Overall, varenicline reduced the number of drinks per day, cravings, and increased abstinent days, but there were no significant differences in percentage of heavy drinking days or abstinence rates.[37] A multicenter RCT investigating the use of varenicline and bupropion for AUD found that the varenicline and varenicline + bupropion groups had significantly lower

phosphatidyl ethanol (PEth) levels (a marker for chronic ethanol consumption) and self-reported heavy drinking days when compared with placebo groups.[38]

Ondansetron: A serotonin 5-HT3 receptor antagonist, and antiemetic has been studied as a potential agent for AUD. An investigation of low-dose ondansetron (0.33 mg PO BID) found that by month six, there were significant reductions in the percentage of monthly heavy drinking days compared to placebo groups.[38] Similar to prazosin, it has also been studied as an agent that can work synergistically with naltrexone and has helped reduce cravings for alcohol.[40]

N-Acetylcysteine: Utilized in acetaminophen toxicity, it modulates synaptic glutamatergic activity and has been studied for use in patients with AUD. In adolescents, it was observed that an eight-week course of 2,400 mg daily was shown to significantly reduce alcohol consumption when compared to placebo, but only in patients with moderate to severe AUD.[41] There are ongoing multicenter RCTs that are further investigating its impact on AUD.[42]

Mifepristone: A glucocorticoid receptor antagonist used for medically induced abortions has also been studied as a potential treatment option for AUD. One study found that 600 mg daily of mifepristone was able to significantly reduce cravings for alcohol when compared to placebo groups.[43] There is currently a clinical trial investigating the utility of mifepristone to prevent relapsing into heavy drinking.