

Pharmacotherapies for Cannabis Use Disorder: Surveillance – January 2022

Objective and Search Period

To identify new eligible randomized controlled trials (RCTs) of pharmacotherapies for cannabis use disorder (CUD), we searched Ovid MEDLINE ALL, PsycINFO, and the Cochrane Database of Systematic Reviews for studies published from **May 2021 to January 2022**.

Surveillance Update

Our updated searches identified 142 unique citations. After review, we included 1 small (N = 72) placebo-controlled RCT of varenicline, a smoking cessation aid, for the treatment of CUD (Table 1).¹ This 6-week pilot study is the first RCT to evaluate varenicline for the treatment of CUD and would be the first smoking cessation aid included in this review. We rated the study as having a moderate risk-of-bias due unclear blinding procedures, attrition, and imbalances in several baseline characteristics (i.e., sex, nicotine smoking status, history of alcohol use disorder) between treatment groups.

During the 6-week treatment period, McRae-Clark and colleagues observed significantly greater reductions in cannabis use, as measured by mean change in urine cannabinoid concentrations, with varenicline compared to placebo (-1.7 ng/mL vs. 1.9 ng/mL; mean difference in change: 3.5 ng/mL [95% CI: 0.1 to 6.9]).¹ In comparison, although investigators observed numerically greater 6-week rates of self-reported abstinence and decreases in cannabis use frequency with varenicline (abstinence: 17.1% vs. 5.4%; mean reduction in % days of cannabis use: -41.7% vs. -27.4%), the between-group differences were not statistically significant.¹ Finally, there were no significant between-group differences in cannabis withdrawal symptoms (e.g., craving) or study-related adverse events.¹ These findings are suggestive of a potential clinical benefit with varenicline in the treatment of CUD; however, due the small sample size and absence of other varenicline trials for comparison, inclusion of this study would not change the overall conclusions of the current review. Therefore, STEM reviewers have determined a formal review update is not warranted at this time.

Table 1. Study Characteristics of New Eligible RCTs of Pharmacotherapies for CUD

Author, Year N Randomized Setting Follow-up Risk of Bias	Population Definition Comorbidity UA Frequency	Drug Class Mechanism of Action	N, Treatment vs. Control Treatment Dose Comparator Concomitant Therapy	Relevant Outcomes
McRae-Clark et al., 2021 ¹ N = 72 Single site (US) 6 weeks Moderate	DSM-5 CUD and using cannabis ≥ 3 days per week NR UA: 2x per week	Smoking cessation aid Nicotine receptor agonist	35 vs. 27 Varenicline (oral tablet) – 2 mg per day PBO (oral tablet) MET (3 sessions) and CM for medication adherence	<ul style="list-style-type: none"> • Abstinence • Cannabis use • Treatment retention • Withdrawal (change in CWS score) • Dropouts due to AE • Serious AE

Abbreviations. AE: adverse events; CUD: cannabis use disorder; CM: contingency management; CWS: Cannabis Withdrawal Scale; MET: motivational enhancement therapy; NR: not reported; PBO: placebo; UA: urinalysis; US: United States

References

1. McRae-Clark AL, Gray KM, Baker NL, et al. Varenicline as a treatment for cannabis use disorder: a placebo-controlled pilot trial. *Drug Alcohol Depend.* 2021;229(Pt B):109111. doi: 10.1016/j.drugalcdep.2021.109111.