A pilot study of the safety and feasibility of oral naltrexone and bupropion for methamphetamine use disorder

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Introduction: A recent study found depot injection naltrexone and oral bupropion, in formulations not readily available internationally, reduced methamphetamine use compared to placebo. We undertook a pilot study to examine an oral formulation.

Methods: A single-arm, open-label, pilot study of oral extended-release naltrexone and bupropion (40mg/450mg daily in divided doses; primary endpoint Day 84) in adults with methamphetamine use disorder. Participants were outpatients of a stimulant treatment program in Sydney, Australia. Participants attended weekly visits from Baseline to Week 12, and received treatment as usual psychosocial therapy, reimbursement was up to $80 for each study visit. Primary outcomes were feasibility (time to recruit, proportion ineligible, retention, and study medication adherence by pill count and self-report), and safety (treatment-emergent adverse events [AEs]).

Results: Over 20 weeks between March and August 2024, 183 expressions of interest were received, 24 individuals were screened, and 20 (83%) enrolled. Adherence by pill count was >80% amongst 46% of participants at the primary endpoint, pill returns were inconsistent across the study. Adherence by self-report was >80% among more than 60% of participants across all visits, and >80% of participants reported at least 80% adherence on seven of the twelve study visits. Fifteen (75%) participants were retained on study medication to primary endpoint. Ninety-three AEs were reported in 19 participants (95%), one (1.1%) was classified serious but unrelated to study medication.

Discussions and Conclusions: Oral combination naltrexone and bupropion was safe in this sample. Adherence aligned with other oral medications trialled in this population, however, did not achieve the rates of adherence in the previous US study using different formulations with smartphone video app and monetary incentives for medication adherence.

Implications for Practice or Policy: This study demonstrates safety and feasibility of this combination in this population, to inform the design of a larger randomised trial.

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