

16. When prescribing psychostimulant medications for StUD, clinicians should maintain a level of monitoring commensurate with the risk profile for the given medication and patient. Monitoring may include pill counts, drug testing, more frequent clinical contact, and more frequent PDMP checks (*Clinical consensus, Strong Recommendation*).

Cocaine Use Disorder

Modafinil

Modafinil is a wakefulness-promoting medication used in the treatment of narcolepsy, obstructive sleep apnea, and shift work-related sleep disorder.¹²⁹ The exact mechanism of action of modafinil is unclear, though in vitro studies have shown that it modulates multiple neurotransmitter systems, including dopamine, serotonin, and norepinephrine reuptake, as well as histamine and hypocretin signaling. Modafinil also activates glutamatergic circuits while inhibiting GABA.^{130,131}

The evidence is mixed regarding the effectiveness of modafinil in reducing cocaine use in patients with cocaine use disorder. Two meta-analyses found no effect on sustained cocaine abstinence but a positive effect on cocaine abstinence rates at the end of the treatment trial in patients treated with modafinil.^{132,133} Notably, many of the studies included in the meta-analyses reported low medication adherence rates. Modafinil has shown more promising efficacy in certain subpopulations, including those without co-occurring AUD and those with high adherence to treatment. The CGC agreed that modafinil may be considered, particularly for patients with higher frequency of cocaine use at the start of treatment.¹³³

Modafinil is generally well tolerated, and the two meta-analyses reported no significant differences in the rate of serious or other adverse events. The CGC noted that modafinil inhibits metabolism of hormonal contraceptives and can reduce the effectiveness of this type of birth control; patients with childbearing potential should be counseled to use an alternative birth control method. Clinicians should generally avoid use of modafinil or psychostimulant medications to treat StUD in patients with histories of psychoses, whether substance-induced or preexisting.¹³⁴

Cocaine Use Disorder: Modafinil Recommendations

17. For patients with cocaine use disorder and without co-occurring AUD, clinicians can consider prescribing modafinil to reduce cocaine use and improve treatment retention (*Low certainty, Conditional Recommendation*).

Please see the supplementary EtD document for the following related summaries of evidence, relevant citations, and CGC judgments: