# Indian Health Service
# National Pharmacy and Therapeutics Committee
# Formulary Brief: *Stimulant Use Disorder*
-August 2022-

## BACKGROUND:

The Indian Health Service (IHS) National Pharmacy and Therapeutics Committee (NPTC) reviewed potential treatment(s) for Stimulant Use Disorder at the August 2022 meeting. This was the NPTC's first review of Stimulant Use Disorder. There are currently no FDA-approved medications for maintenance treatment of this condition. The Agency for Healthcare Research and Quality (AHRQ) recommends bupropion, methylphenidate, mirtazapine, naltrexone, and topiramate.[1] Currently, bupropion, methylphenidate, naltrexone, and topiramate are listed on the IHS National Core Formulary (NCF). At the conclusion of the review, the NPTC made **no modifications to the NCF**.

## Discussion:

The age-adjusted rate of overdose deaths attributed solely to psychostimulants has increased by a factor of 10 from 2009 to 2019.[2] Prescription stimulant misuse among AI/AN increased in ages 12-17 and 18-25.[3] Though rates of methamphetamine misuse for those ages 26 years and older are slightly higher than other age groups, there has been a decline in cocaine and methamphetamine misuse among AI/AN overall from 2017 to 2019.[4]

Stimulant misuse is mediated by dopamine release in the mesolimbic reward pathway and neural activity in the ventral tegmental area projecting into the nucleus accumbens.[5] Although cocaine and amphetamine-type stimulants (e.g., methamphetamine and prescription stimulants) cause serotonin, norepinephrine and dopamine to be released, their specific action on dopamine results in euphoria and can perpetuate further misuse of the stimulant. Like cocaine, methamphetamine (MA) can block re-entry of dopamine back into the pre-synaptic neuron (cocaine $T_{1/2}$ = 1hr). However, unlike cocaine, MA can cross the neuronal cell membrane and enter the presynaptic neuronal vesicles that store dopamine causing damage and leakage into the synaptic cleft. Large amounts of dopamine in the synapse for prolonged periods of time can cause the post-synaptic neuron to be activated to dangerously high levels causing the user to experience a powerful feeling of euphoria (MA $T_{1/2\text{- smoked}}$ =8-12 hours)[5]. Because stimulants exert their effects in a dose-dependent manner, the route of administration has serious neurologic, physical, psychiatric, and neurocognitive implications for the person using the stimulant.

**Screening tools:** There are no universal screening tools that exist for Stimulant Use Disorder and routine urine drug screening (UDS) is not recommended for the general population. High risk populations such as pregnant women, men who have sex with men (MSM), those accessing substance use treatment or reporting past or current use of illicit substances, or patients presenting in areas/settings with high MA use should be asked about MA use as a part of substance use history.[6]

**Acute Intoxication Management:** Stimulant use results in euphoria, hyper-excitability, hypersexuality, locomotor activity, agitation and psychotic symptoms, including paranoia and hallucinations. Management of acute stimulant intoxication is largely supportive using non-pharmacologic de-escalation. For example, if a patient presents with acute agitation, it is best to move the patient to a quiet, safe, low-stimulus and calm environment. However, if non-pharmacologic de-escalation is inadequate or if there are concerns for safety, consider the following pharmacological treatment: [7,8]

**Preferred for acute management of agitation and distress**: lorazepam 1-2mg PO, IM or IV
**Adjunctive for acute management of agitation and distress**, especially if patient is experiencing psychosis/ paranoia/ hallucinations: *[*Available as an Orally Disintegrating Tablet]*

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|---|---|---|
| Risperidone* 1-2mg PO | Haloperidol 5mg PO or 5-10mg IM | Olanzapine* 10mg PO or 5-10mg IM |

**Stimulant Withdrawal Management:** Stimulant withdrawal is defined as a patient that displays dysphoric mood and ≥2 of the following: fatigue, vivid/unpleasant dreams, insomnia or hypersomnia, increased appetite, psychomotor retardation or agitation.[9,10] Pharmacotherapy is not recommended. Management for withdrawal is supportive.[11]

**Psychosocial Clinical Interventions:** Current evidence supports psychosocial evidence-based interventions such as motivational interviewing, contingency management (CM), community reinforcement approach (CRA), and cognitive behavioral therapy (CBT).[12]

**Potential Maintenance Psycho-pharmacotherapy:** A review of currently available literature guided by AHRQ recommendations was the strategy utilized as there were no guidelines that had recommendations for psycho-pharmacotherapy for maintenance treatment for Stimulant Use Disorder.

A systematic review and meta-analysis of 48 randomized controlled trials (RCTs) and 7 systematic reviews (SR) examined whether 66 medications compared head-to-head or compared to placebo or psychotherapy, had an effect on sustained abstinence from cocaine as evidenced by ≥ 3 weeks of negative UDS.[13] Overall, the authors concluded that there is no strong or consistent evidence that any drug class is effective in increasing abstinence, reducing use or improving treatment retention.

In a Cochrane review of 14 RCTs in adults (n=719) with ≥18 years of cocaine dependency, the antipsychotics risperidone, olanzapine, quetiapine, lamotrigine, aripiprazole, haloperidol, and reserpine, alone or in combination with any psychosocial intervention vs placebo, no intervention, or other pharmacological or psychosocial interventions were assessed.[14] The study authors concluded that evidence is lacking that supported the clinical use of antipsychotic medications for treatment of cocaine evidence and that quetiapine results looked promising but low sample size limited its generalizability.

Psychostimulants for use in amphetamine abuse or dependence were also reviewed. In a Cochrane Review of 11 RCTs, psychostimulants (dexamphetamine, bupropion XL, methylphenidate, and modafinil) were compared to placebo.[15] The authors concluded that the review did not support the use of psychostimulants as replacement therapy for amphetamine abuse or dependence.

In a meta-analysis of 17 RCTs of adults with MA or amphetamine disorder, pharmacotherapy (antidepressants, antipsychotics, muscle relaxants/anticonvulsants, naltrexone, varenicline, atomoxetine, ondansetron, dexamphetamine, methylphenidate, modafinil) was compared head-to-head, to placebo or versus psychotherapy.[16] The authors concluded that psychostimulants had no statistically significant effect on abstinence and retention, although methylphenidate may more effective than placebo in reducing amphetamine use.

**Findings:**

Heterogeneity in trials, low sample sizes, high rates of attrition in a majority of studies, and low representation of women limits the possibility of drawing conclusions and generalizing the findings. There is a lack of conclusive evidence to recommend methylphenidate or topiramate. Based on subject matter expertise from field clinicians who work with Substance Use Disorder populations, the first choice for treatment of Substance Use Disorder is bupropion especially if the client has weight concerns. Mirtazapine can also be used as an alternate treatment although weight gain is more probable. Naltrexone can be used as add-on therapy, especially if alcohol use is involved.

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*If you have any questions regarding this document, please contact the NPTC at IHSNPTC1@ihs.gov. For more information about the NPTC, please visit the NPTC website.*

**References:**


1. Agency for Healthcare Research and Quality (AHRQ). Stimulant Use Disorder and Behavioral Health Integration. Accessed July 2022.
2. Hedegaard H, Miniño AM, Warner M. Co-involvement of opioids in drug overdose deaths involving cocaine and psychostimulants. NCHS Data Brief, no 406. Hyattsville, MD: National Center for Health Statistics. 2021 April 01.
3. Center for Behavioral Health Statistics and Quality. Results from the 2020 National Survey on Drug Use and Health: Graphics from the Key Findings Report. Substance Abuse and Mental Health Services Administration.2020.
4. SAMHSA. 2019 National Survey on Drug Use and Health: American Indian and Alaska Natives. Accessed July 2022.
5. SAMHSA. Treatment for Stimulant Use Disorders. Treatment Improvement Protocol (TIP) Series 33. SAMHSA Publication No. PEP21-02-01-004. Rockville, MD: Substance Abuse and Mental Health Services Administration, 2021.
6. Gasper J, Puzantian T. Pharmacist Toolkit: Methamphetamine Use Disorder. *College of Psychiatric and Neurologic Pharmacists*, 2020.
7. Wodarz N, Krampe-Scheidler A, Christ M, et al. Evidence-Based Guidelines for the Pharmacological Management of Acute Methamphetamine-Related Disorders and Toxicity. Pharmacopsychiatry. 2017;50(3):87-95.
8. Härtel-Petri R, et al. Evidence-Based Guidelines for the Pharmacologic Management of Methamphetamine Dependence, Relapse Prevention, Chronic Methamphetamine-Related, and Comorbid Psychiatric Disorders in Post-Acute Settings. Pharmacopsychiatry. 2017;50(3):96-104.
9. Agency for Healthcare Research and Quality. Stimulant Use Disorder and Behavioral Health Integration. Accessed July 20, 2022.
10. American Psychiatric Association: Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition. Am Psych Assoc. (2013): 561-570.
11. SAMHSA. Treatment of Stimulant Use Disorders. SAMHSA Publication No. PEP20-06-01-001 Rockville, MD: National Mental Health and Substance Use Policy Laboratory. Substance Abuse and Mental Health Services Administration, 2020.
12. Bhatt M, Zielinski L, Baker-Beal Lola, et al. Efficacy and Safety of psychostimulants for amphetamine and methamphetamine use disorder: A systematic review and meta-analysis. *Syst Rev.* 2016; 5:189.
13. Chan B, Kondo K, Freeman M, et al. Pharmacotherapy for Cocaine Use Disorder. J Gen Intern Med. 2019; 34(12): 2858-73.
14. Indave BI, Minozzi S, Pani PP, et al. Antipsychotic medications for cocaine dependence. *Cochrane Database Syst Rev.* 2016,3, No:CD006306.
15. Pérez-Mañá C, Castells X, Torrens M, et al. Efficacy of psychostimulant drugs for amphetamine abuse or dependence (Review). *Cochrane Database Syst Rev* 2013, Issue 9. Art. No:CD009695.
16. Chan B, Freeman M, Kondo K, et al. Pharmacotherapy for methamphetamine/amphetamine use disorder- a systematic review and meta-analysis. *Addiction.* 2019; 114:2122-36.