Indian Health Service
National Pharmacy and Therapeutics Committee
Formulary Brief: ***Treatment of Adult ADHD***
-April 2025-

Background:

The Indian Health Service (IHS) National Pharmacy and Therapeutics Committee (NPTC) reviewed the treatment of attention-deficit/hyperactivity disorder (ADHD) in adults at the Spring 2025 quarterly meeting. Medications on the National Core Formulary (NCF) for ADHD treatment include both immediate and extended-release formulations of methylphenidate and dextroamphetamine/amphetamine, atomoxetine, and bupropion. This review marks the NPTC's initial evaluation of ADHD treatment for adult patients. Following the comprehensive review in adult patients, the NPTC voted to **remove the "Pediatric Use Only" language for ADHD medications** currently listed on the NCF.

Discussion:

ADHD, a neurodevelopmental disorder, characterized by symptoms of impaired attention, hyperactivity, and impulsivity develops during childhood and can span throughout adulthood.[1-3] The prevalence of ADHD is estimated in U.S. adults to be 15.5 million (6%), of which over-half (55.9%) received an ADHD diagnosis when they were ≥18 years old.[1] Globally, approximately 2-5% of adults experience ADHD symptoms.[1]

ADHD often persists into adulthood with hyperactive symptoms usually manifesting in a more subtle way and inattentive symptoms persisting. Undiagnosed ADHD may emerge more clearly in adults with the increasing demands of higher learning, work, or family responsibilities. ADHD is thought to be under-recognized and underdiagnosed in females. Lastly, initiation of ADHD medications (stimulants and non-stimulants) in adults has been associated with a reduction in mortality from accidental injuries and other unnatural causes.[19]

Adults with ADHD often have comorbid mental health conditions which can present both diagnostic and treatment challenges.[17] Adult ADHD is associated with a 5-fold increased risk for anxiety disorders, a 4.5-fold increased risk for major depression, an 8.7-fold increased risk for bipolar disorder, and a 4.6-fold increased risk for substance use disorders.[4] The impact of ADHD on the level of functional impairment, in all aspects of family, work and social contexts can vary in severity, be limited to certain settings, and cause minimal impairment in other settings.[1,5-10] Ensuring the appropriate diagnosis of ADHD is key to treatment and requires a substantial amount of time and interviews with the patient and key family members; screening tools (e.g., DIVA-5, ASRS v1.1) may be used to guide clinicians with symptom assessment in conjunction with an extensive clinical interview.[11]

Current Australian, British, and Canadian guidelines as well as the American Academy of Family Physicians and the U.S. Veterans Health Administration recommendations concur that stimulants are the mainstay of ADHD treatment in adults.[5-9] Current U.S. guidelines are undergoing review by the American Professional Society for ADHD and Related Disorders with release expected in the fourth quarter of 2025.[10]

Diversion of prescription stimulants for nonmedical use is a concern. However, data shows that nonmedical use of stimulants has remained stable for the past 20 years, and the most common source of prescription stimulants for non-medical use are family or friends.[12] The risk of diversion must be carefully weighed with behavioral problems that may persist without treatment as well as the associated risk of morbidity and mortality. In a large-scale Dutch study of adolescents ages 12 to 18, national prescription data was linked to a database of minor offenses; consistent ADHD adherence was associated with lower risk of committing minor offenses (e.g., trespassing, property crimes, destruction or disorderly conduct), HR 0.67, 95% CI: 0.64-0.71, $p<0.001$.[18]

Current studies of adult ADHD tend to be heterogeneous, low-quality studies due to high risk of bias. In a 2020 systematic review and network meta-analysis which evaluated pharmacologic treatments (methylphenidate, atomoxetine, mixed amphetamine salts, bupropion, dexamphetamine, and guanfacine) compared to placebo for adults with ADHD, showed that the number of patients who demonstrated a clinical response was higher among those using any ADHD pharmacotherapy at 12 weeks (RR 1.32, 95% CI: 1.05 to 1.66, I^2=58%).[13]

However, when only studies at low risk of bias were assessed, these findings were not sustained.[13] Atomoxetine compared to placebo was associated with improved patient-reported clinical response.[13]

A 2021 Cochrane Review, which evaluated the efficacy and safety of IR methylphenidate, reported that low-certainty evidence showed that IR methylphenidate (when compared to placebo) may reduce ADHD symptoms using the Adult ADHD Investigator Symptom Report Scale (score 0 to 54), (MD = -20.7; 95% CI: -23.9 to -17.4).[14] IR methylphenidate increased risk of gastrointestinal complications (RR 1.96, 95% CI: 1.13 to 2.95) and loss of appetite (RR 1.77, 95% CI: 1.06 to 2.96), and there were inconsistent reports on cardiovascular events which did not allow for analysis. In a 2022 Cochrane Review on the efficacy and harms of ER formulations of methylphenidate vs. placebo, low certainty evidence showed that ER methylphenidate had no effect on serious adverse effects (RR 1.43, 95% CI: 0.85 to 2.43). ER methylphenidate did improve self-rated ADHD symptoms (small-to-moderate effect; SMD -0.37, 95% CI: -0.43 to -0.30), self-rated quality of life (small effect; SMD -0.15, 95% CI: -0.25 to -0.05), investigator-rated ADHD symptoms (small-to-moderate effect; SMD -0.42, 95% CI: -0.49 to -0.36), and ADHD symptoms rated by peers and family members (small-to-moderate effect; SMD -0.31, 95% CI -0.48 to -0.14).[15]

Findings:

Based on current available evidence and guidelines, central nervous stimulants should be considered first-line for adults with ADHD who possess neither contraindication(s) nor a current stimulant use disorder. Nonstimulants, such as atomoxetine, may be considered if stimulants are ineffective or if the patient has a current stimulant use disorder. At present, there is not enough supportive data to recommend lisdexamfetamine in adults and the FDA's boxed warning on its high potential for abuse and misuse should be considered.[16] Overall, treatment for adults with ADHD should be patient-tailored and take into account the presence of other mental health comorbidities.

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.

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