

Therapeutic Class Overview Attention Deficit/Hyperactivity Disorder (ADHD) Agents

Therapeutic Class Overview/Summary:

This review will focus on the agents used in the treatment of attention deficit/hyperactivity disorder (ADHD). These agents come from a variety of drug classes and are summarized in Table 1.¹⁻²⁷ ADHD is a common psychiatric disorder often diagnosed during childhood; however, children with ADHD may continue to manifest symptoms into adulthood.^{28,29} The core symptoms of ADHD utilized in the diagnosis of the disorder include hyperactivity, impulsivity and inattention. There are three subtypes of ADHD, including a predominantly inattentive subtype, a predominantly hyperactive-impulsive subtype and a combined subtype in which both symptoms are displayed.^{28,29} Untreated, or undertreated, ADHD is associated with adverse sequelae, including delinquent behavior, antisocial personality traits, substance abuse and other comorbidities²⁹. There are several central nervous system agents that are Food and Drug Administration (FDA)-approved for the treatment of ADHD, including the cerebral stimulants (amphetamines and methylphenidate derivatives), as well as atomoxetine (Strattera[®]), clonidine extended-release (Kapvay[®]) and guanfacine extended-release (Intuniv[®]).¹⁻²⁷ Due to the potential for abuse, the cerebral stimulant agents are classified as Schedule II controlled substances.¹⁻²⁴ Atomoxetine, clonidine extended-release and guanfacine extended-release are not classified as controlled substances.²⁵⁻²⁷ Clonidine and guanfacine extended-release formulations are approved for use as both adjunctive therapy with stimulant medications and as monotherapy.^{26,27}

Most ADHD agents and stimulants are currently available generically. Agents that are available only as a brand name product include: lisdexamfetamine capsules (Vyvanse[®]), amphetamine tablets (Evekeo[®]), orally disintegrating tablets (Adzenys XR-ODT[®]), and extended-release suspension (Dyanavel XR[®]), atomoxetine capsules (Strattera[®]), methylphenidate patch (Daytrana[®]), extended release chewable tablet (Quillichew[®]), and extended-release suspension (Quillivant XR[®]). Aptensio XR[®] (methylphenidate extended-release capsule) is also available only as a brand name product; however, other extended-release biphasic capsules are available generically.³¹

Current consensus clinical guidelines for the treatment of children and adolescents with ADHD recommend that stimulants are highly effective for reducing core symptoms of ADHD in children.^{29,30,32} Although initial therapy with atomoxetine or extended-release formulations of clonidine and guanfacine may reduce core symptoms of ADHD, there is less evidence to support their use compared to stimulants. The selection of therapy should be based on comorbid conditions, adverse event profiles, compliance issues, risk of drug diversion and patient/parent preference.³³ Stimulants, particularly methylphenidate, are recommended as first-line therapy in adult patients with ADHD.^{30,34} Consensus guidelines also list these agents as options in the treatment of narcolepsy.³⁵⁻³⁷

Table 1. Current Medications Available in the Therapeutic Class¹⁻²⁷

Generic (Trade Name)	Food and Drug Administration-Approved Indications	Dosage Form/Strength	Generic Availability
Anorexigenic Agents and Respiratory and Cerebral Stimulants-Amphetamines			
Amphetamine (Adzenys XR-ODT [®] , Dyanavel XR [®] , Evekeo [®])	Treatment of ADHD, narcolepsy [†] , exogenous obesity [†]	Extended-release suspension 2.5 mg/mL Tablet: 5 mg 10 mg	-
Amphetamine/dextroamphetamine salts (Adderall ^{®*} , Adderall XR ^{®*})	Treatment of ADHD, narcolepsy [‡]	Capsule: 5 mg 10 mg 15 mg	✓

Generic (Trade Name)	Food and Drug Administration- Approved Indications	Dosage Form/Strength	Generic Availability
		20 mg 25 mg 30 mg Extended-release orally disintegrating tablet: 3.1 mg 6.3 mg 9.4 mg 12.5 mg 15.7 mg 18.8 mg Tablet: 5 mg 7.5 mg 10 mg 12.5 mg 15 mg 20 mg 30 mg	
Dextroamphetamine (ProCentra ^{®*} , Dexedrine ^{®*} , Dexedrine Spansule ^{®*} , Zenzedi ^{®*})	Treatment of ADHD, narcolepsy	Solution: 5 mg/5 mL Sustained-release capsule: 5 mg 10 mg 15 mg Tablet: 2.5 mg 5 mg 7.5 mg 10 mg	✓
Lisdexamfetamine (Vyvanse [®])	Treatment of ADHD, binge eating disorder [§]	Capsule: 10 mg 20 mg 30 mg 40 mg 50 mg 60 mg 70 mg	-
Methamphetamine (Desoxyn ^{®*})	Treatment of ADHD, exogenous obesity	Tablet: 5 mg	✓
Anorexigenic Agents and Respiratory and Cerebral Stimulants-Miscellaneous			
Dexmethylphenidate (Focalin ^{®*} , Focalin XR ^{®*})	Treatment of ADHD	Extended-release capsule: 5 mg 10 mg	✓

Generic (Trade Name)	Food and Drug Administration- Approved Indications	Dosage Form/Strength	Generic Availability
		15 mg 20 mg 25 mg 30 mg 35 mg 40 mg Tablet: 2.5 mg 5 mg 10 mg	
Methylphenidate (Aptensio XR [®] , Concerta ^{®*} , Daytrana [®] , Metadate CD ^{®*} , Metadate ER ^{®*} , Methylin ^{®*} , Methylin ER ^{®*} , Quillichew ER [®] , Quillivant XR [®] , Ritalin ^{®*} , Ritalin LA ^{®*} , Ritalin SR ^{®*})	Treatment of ADHD, narcolepsy [¶]	Chewable tablet: 2.5 mg 5 mg 10 mg Extended-release capsule (Aptensio XR [®]) 10 mg 15 mg 20 mg 30 mg 40 mg 50 mg 60 mg Extended-release capsule (Metadate CD [®] , generic): 10 mg 20 mg 30 mg 40 mg 50 mg 60 mg Extended-release capsule (Ritalin LA [®] , generic): 10 mg 20 mg 30 mg 40 mg Extended-release chewable tablet: 20 mg 30 mg 40 mg Extended-release	✓

Generic (Trade Name)	Food and Drug Administration-Approved Indications	Dosage Form/Strength	Generic Availability
		suspension: 25 mg/ 5 mL Extended-release tablet (Concerta [®] , generic): 18 mg 27 mg 36 mg 54 mg Extended-release tablet (Metadate ER [®] , generic): 10 mg 20 mg Solution: 5 mg/5 mL 10 mg/5 mL Sustained-release tablet (Ritalin SR [®] , generic): 20 mg Tablet: 5 mg 10 mg 20 mg Transdermal patch: 10 mg/9 hours (1.1 mg/hour) 15 mg/9 hours (1.6 mg/hour) 20 mg/9 hours (2.2 mg/hour) 30 mg/9 hours (3.3 mg/hour)	
Central α-Agonists			
Clonidine extended-release (Kapvay ^{®*})	Treatment of ADHD	Extended-release tablet: 0.1 mg 0.2 mg	✓
Guanfacine extended-release (Intuniv ^{®*})	Treatment of ADHD	Extended-release tablet: 1 mg 2 mg 3 mg 4 mg	✓
Central Nervous System Agents-Miscellaneous			

Generic (Trade Name)	Food and Drug Administration-Approved Indications	Dosage Form/Strength	Generic Availability
Atomoxetine (Strattera®)	Treatment of ADHD	Capsule: 10 mg 18 mg 25 mg 40 mg 60 mg 80 mg 100 mg	-

ADHD=attention deficit hyperactivity disorder

*Generic available in at least one dosage form or strength.

†Evekeo®

‡Adderall®

§For use in moderate to severe binge eating disorder. Not indicated for weight loss or treatment of obesity.

|| Metadate ER®, Methylin®, Ritalin® and Ritalin SR®

Evidence-based Medicine

- The attention deficit/hyperactivity disorder (ADHD) agents and stimulants have demonstrated the safety and efficacy for their Food and Drug Administration (FDA)-approved indications.³⁹⁻¹³²
- Overall, there is insufficient evidence to suggest that one ADHD agent and stimulant is more efficacious than another for the treatment of ADHD.³⁹⁻¹³²
- Limited data exists to demonstrate the efficacy of a variety of cerebral stimulants and atomoxetine in the adult population.^{44,46,52-54, 62,63,71,90,93,98,99,101,104,113,114,116}

Key Points within the Medication Class

- According to Current Clinical Guidelines:
 - Current consensus clinical guidelines for the treatment of children and adolescents with ADHD recommend that stimulants are highly effective for reducing core symptoms of ADHD in children.^{29,30,32}
 - Although initial therapy with atomoxetine or extended-release formulations of clonidine and guanfacine may reduce core symptoms of ADHD, there is less evidence to support their use compared to stimulants. The selection of therapy should be based on comorbid conditions, adverse event profiles, compliance issues, risk of drug diversion and patient/parent preference.³³
 - Stimulants, particularly methylphenidate, are recommended as first-line therapy in adult patients with ADHD.^{31,34}
- Other Key Facts:
 - At least one short-, intermediate-, and long-acting stimulant is available generically.²⁹

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