

## Stimulants for ADHD

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Optimizing ADHD Diagnosis

ADHD diagnosis is based on DSM-5 criteria for children, adolescents and adults. If DSM-5 criteria is not met, consider alternative diagnoses or refer to an appropriate subspecialist. If an ADHD diagnosis is made, consider evidence of comorbid conditions such as anxiety, learning disorder, and trauma and perform additional screening as indicated prior to selecting treatment options.

Refer to Clinical Practice Resources: [MCMS ADHD Guideline](#), [AAP ADHD Guideline](#), and [DSM -5 Criteria \(Table 1 Below\)](#)

Selecting a Stimulant

Stimulants are considered first-line agents for the treatment of uncomplicated ADHD in ages >5 years. In most systematic reviews, methylphenidate, dexamethylphenidate, and amphetamines are rated equally efficacious and safe. There is, however, some evidence to support that treatment with mixed dextroamphetamine-amphetamine salts may be associated with a greater decrease in weight over time, risk of irritability, and higher abuse potential compared to methylphenidate. Guidelines from the AAP and AACP do not endorse preference for one stimulant over another.

With definitive comparative data lacking, the best strategy is often to select and trial an agent, and then select and trial another agent if the initial choice isn't effective (after optimizing dosage and frequency of dosing with an adequate trial period of at least 30 days), tolerated, or covered by insurance. **The choice of an initial stimulant agent should be based on age, duration of effect, side effects and comorbidities, ability to swallow, patient/caregiver preference and cost/coverage.**

See Table 2 for a comparison of dosage form, dosing frequency, duration of action and cost of many stimulants.

**Stimulant Prescribing Message** ADHD medications constitute the highest pharmacy spend category for primary care pediatrics. In general, brand stimulant products are more costly than generic agents in this drug category. Vyvanse is one example, ranking as the 6<sup>th</sup> most expensive brand agent for overall spend across the AHP network. **When stimulants are medically indicated, we recommend providers uniformly begin treatment with generic stimulants whenever possible.**

Making Stimulant Cost Comparisons

- Generic stimulants are generally less expensive than brand; however, generics are not available for all drug formulations. When a product is available as brand only, weigh against comparable products:
  - Adzenys XR ODT and Dyanavel XR Suspension are once-daily extended release amphetamine products that offer utility in patients unable to swallow tabs/caps with a duration of activity of up to 12 hours. However, in this scenario we suggest using *generic* Adderall XR capsules which has a clinically similar duration of action, can be sprinkled on applesauce, and monthly cost is 70-140% lower.

**Vyvanse** is a prodrug converted to its active form (dextroamphetamine) through first pass metabolism after oral ingestion, designed to discourage misuse. This benefit is theoretical and there is no RCT data proving a lower abuse potential.

Consider prescribing generic long-acting stimulant agents preferentially (e.g., *generic* Concerta or Adderall XR), reserving Vyvanse as an alternative.

## Table 1: DSM-5 Diagnostic Criteria for ADHD

### A. A persistent pattern of inattention and/or hyperactivity-impulsivity that interferes with functioning or development as characterized by (1) and/or (2):

1. **Inattention:** Six (or more) of the following symptoms have persisted for at least 6 months to a degree that is inconsistent with developmental level and that negatively impacts directly on social and academic/occupational activities:

**NOTE:** The symptoms are not solely a manifestation of oppositional behavior, defiance, hostility, or failure to understand tasks or instructions. For older adolescents and adults (age 17 and older), at least five symptoms are required.

- a. Often fails to give close attention to details or makes careless mistakes in schoolwork, at work, or during other activities (e.g., overlooks or misses details, work is inaccurate).
- b. Often has difficulty sustaining attention in tasks or play activities (e.g., has difficulty remaining focused during lectures, conversations, or lengthy reading).
- c. Often does not seem to listen when spoken to directly (e.g., mind seems elsewhere, even in the absence of any obvious distraction).
- d. Often does not follow through on instructions and fails to finish schoolwork, chores, or duties in the workplace (e.g., starts tasks but quickly loses focus and is easily sidetracked).
- e. Often has difficulty organizing tasks and activities (e.g., difficulty managing sequential tasks; difficulty keeping materials and belongings in order; messy, disorganized work; has poor time management; fails to meet deadlines).
- f. Often avoids, dislikes or is reluctant to engage in tasks that require sustained mental effort (e.g., schoolwork or homework; for older adolescents and adults, preparing reports, completing forms, reviewing lengthy papers).
- g. Often loses things necessary for tasks or activities (e.g., school materials, pencils, books, tools, wallets, keys, paperwork, eyeglasses, or mobile telephones).
- h. Is often easily distracted by extraneous stimuli (for older adolescents and adults, may include unrelated thoughts).
- i. Is often forgetful in daily activities (e.g., doing chores, running errands; for older adolescents and adults, returning calls, paying bills, or keeping appointments).

2. **Hyperactivity and Impulsivity:** Six (or more) of the following symptoms have persisted for at least 6 months to a degree that is inconsistent with developmental level and that negatively impacts directly on social and academic/occupational activities:

**NOTE:** The symptoms are not solely a manifestation of oppositional behavior, defiance, hostility, or failure to understand tasks or instructions. For older adolescents and adults (age 17 and older), at least five symptoms are required.

- a. Often fidgets or taps hands or feet or squirms in seat.
- b. Often leaves seat in situations when remaining seated is expected (e.g., leaves his or her place in the classroom, in the office or other workplace, or in other situations that require remaining in place).
- c. Often runs about or climbs in situations where it is inappropriate. (**NOTE:** In adolescents or adults, may be limited to feeling restless).
- d. Often unable to play or engage in leisure activities quietly.
- e. Is often "on the go," acting as if "driven by a motor" (e.g., is unable to be or uncomfortable being still for extended time, as in restaurants, meetings; may be experienced by others as being restless or difficult to keep up with).
- f. Often talks excessively.
- g. Often blurts out an answer before a question has been completed (e.g., completes people's sentences; cannot wait for turn in conversation).
- h. Often has difficulty waiting his or her turn (e.g., while waiting in line).
- i. Often interrupts or intrudes on others (e.g., butts into conversations, games, or activities; may start using other people's things without asking or receiving permission; for adolescents and adults, may intrude into or take over what others are doing).

#### **In addition, the following conditions must be met:**

- B. Several inattentive or hyperactive-impulsive symptoms were present prior to age 12 years.
- C. Several inattentive or hyperactive-impulsive symptoms are present in two or more settings (e.g., at home, school or work; with friends or relatives; in other activities).
- D. There is clear evidence that the symptoms interfere with or reduce the quality of social, academic, or occupational functioning.
- E. The symptoms do not occur exclusively during the course of schizophrenia or another psychotic disorder and are not better explained by another mental disorder (e.g., mood disorder, anxiety disorder, dissociative disorder, personality disorder, substance intoxication or withdrawal).

## Table 2: Comparison of Stimulant Drug Characteristics and Cost

Generic Name	Brand Name	Dosage Forms <sup>2</sup>	Average Monthly Cash Price*	Dosing Frequency	Duration of Action <sup>1</sup>
<b>Short-acting methylphenidate type products</b>					
Methylphenidate HCL	Ritalin	Tablets	\$85	BID – TID	3-5 hrs
Methylphenidate HCL	Methylin	Chew tabs Solution	\$385 \$210	BID – TID	3-5 hrs
Dexmethylphenidate HCL	Focalin	Tablets	\$90	BID	3-5 hrs
<b>Intermediate to Long-acting methylphenidate type products</b>					
Methylphenidate HCL ER	Metadate ER	ER Tablets	\$165	Daily	8 hrs
Methylphenidate HCL ER (CD) <sup>1</sup>	Metadate CD	ER Capsules	\$157	Daily	6-8 hrs
Methylphenidate HCL ER (LA) <sup>1</sup>	Ritalin LA	ER Capsules	\$169	Daily	6-8 hrs
Dexmethylphenidate HCL ER (XR) <sup>3</sup>	Focalin XR	ER Capsules	\$213	Daily	8-12 hrs
Methylphenidate HCL ER	QuilliChew ER	ER Chew Tabs	<b>Brand only \$399</b>	Daily	8 hrs
Methylphenidate HCL ER (XR)	Quillivant XR	ER Suspension	<b>Brand only \$280</b>	Daily	12 hrs
Methylphenidate HCL ER	Concerta	ER Tablets	\$240	Daily	12 hrs
Methylphenidate transdermal system	Daytrana	Patch	<b>Brand only \$400</b>	Daily (worn for 9 hours)	12 hrs
Methylphenidate HCL ER (XR) <sup>3</sup>	Aptensio XR	ER Capsules	<b>Brand only \$251</b>	Daily	12 hrs
<b>Short-acting amphetamine type products</b>					
Dextroamphetamine + amphetamine	Adderall	Tablets	\$91	Daily - TID	6 hrs, dose dependent
Dextroamphetamine sulfate	Zenzedi	Tablets	Generic: 5 & 10 mg \$162 <b>Brand only: 2.5, 7.5, 15, 20, 30 mg \$430</b>	Daily - BID	4-6 hrs
Dextroamphetamine sulfate ER	Dexedrine Spansule SR	ER Capsules	\$274	Daily - BID	6-8 hrs
Amphetamine sulfate	Evekeo	Tablets	\$332	Daily - TID	9 hrs
<b>Intermediate to Long-acting amphetamine type products</b>					
Dextroamphetamine + amphetamine ER (XR) <sup>3</sup>	Adderall XR	ER Capsules	\$201	Daily	10-12 hrs
Lisdexamphetamine <sup>4</sup>	Vyvanse	Capsules Chew tabs	<b>Brand only \$367</b>	Daily	10 hrs
Amphetamine ER (XR)	Dyanavel XR	ER Suspension	<b>Brand only \$668</b>	Daily	12 hrs
Amphetamine ER (XR)	Adzenys XR	ER ODT	<b>Brand only \$1,450</b>	Daily	10-12 hours

\*www.goodrx.com as of November 2018; prices will vary based on individual insurance coverage, product manufacturer, pharmacy, strength, and month supply; <https://www.goodrx.com/central-nervous-system-stimulants> <sup>1</sup>Onset of action is similar (20-60 minutes) across products, <sup>2</sup>ER products should not be crushed, chewed, or divided. <sup>3</sup>Can sprinkle on applesauce; <sup>4</sup>Can dissolve in water, OJ, yogurt