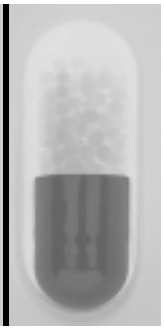
# Stimulants and Nonstimulants for ADHD



**Stimulants**

Adderall and Adderall XR (amphetamine mixtures)
Concerta (methylphenidate, extended release)
Daytrana (methylphenidate topical patch)
Dexedrine and Dexedrine Spansules (dextroamphetamine)
Focalin and Focalin XR (dexmethylphenidate, immediate and extended release)
Metadate ER and and Metadate CD (methylphenidate, extended release)
Ritalin, Ritalin-SR, and Ritalin LA (methylphenidate, immediate and extended release)
Vyvanse (lisdexamfetamine)

**Nonstimulants**

Catapres (clonidine)
Strattera (atomoxetine)
Tenex (guanfacine)

The psychostimulants, more simply known as stimulants, are used primarily in treating attention-deficit/hyperactivity disorder (ADHD) and narcolepsy, a condition characterized by daytime somnolence in which the patient periodically falls into a deep sleep during the day. Narcolepsy is a disorder of the sleep–wake control mechanisms within the brain that interferes with both daytime wakefulness and nighttime sleep.

Other medications used in the treatment of ADHD are the so-called nonstimulants. This mixed group of medications is unlike the stimulants, and there is not the concern of abuse and dependence with these medications as with amphetamines and methylphenidate. The only nonstimulant approved by the U.S. Food and Drug Administration (FDA) for treatment of ADHD is Strattera (atomoxetine). The other nonstimulants, including Tenex (guanfacine), Catapres (clonidine), and Wellbutrin (bupropion), are not approved by the FDA for treatment of ADHD, and they are prescribed "off-label." The use of a medication for its approved indications is called its *labeled use*. In clinical practice, however, physicians often prescribe medications for *unlabeled* (off-label) uses when published clinical studies, case reports, or their own clinical experiences support the efficacy and safety of those treatments.

For those who do not like to take pills, methylphenidate can be introduced into circulation through the skin by a topical patch. The methylphenidate topical patch, called Daytrana, can be worn for up to 9 hours to deliver a controlled rate of methylphenidate through the skin. After absorption of the medication into circu-

lation, there is no difference in the action of the medication than had it been taken orally. For more information on Daytrana, refer to the handout for this medication.

**Vyvanse (lisdexamfetamine)** is a unique extended-release formulation of dextroamphetamine, or *d*-amphetamine. The extended release is accomplished through modification of the active molecule dextroamphetamine to form lisdexamfetamine, which is inactive. After Vyvanse is taken, it is rapidly absorbed and distributed to the liver, where it is converted back to the active stimulant, *d*-amphetamine. The time to absorb and convert lisdexamfetamine to dextroamphetamine essentially makes Vyvanse an extended-release formulation of *d*-amphetamine. For more information on Vyvanse, refer to the handout for this medication.

In numerous clinical studies and decades of clinical experience, the stimulants have clearly demonstrated improvement of outcome for children with ADHD. They increase children's ability to concentrate, extend their attention span, and decrease hyperactivity. Adults with ADHD also benefit from therapy with stimulants. Stimulants help adults concentrate and remain focused on their tasks, increase their attention span, and decrease impulsivity and hyperactivity.

The nonstimulants are not as commonly used as the amphetamines and methylphenidate for ADHD. Except for Strattera, the nonstimulants have not been widely studied for treatment of ADHD, and evidence of their effectiveness is, at best, based on limited clinical trials but mostly clinical experience.

## Dosing Information

Dosing of stimulants in adults is based on clinical presentation and individualized to the patient's response and reported side effects. In children, dosing is also based on age and weight. The other consideration in dosing is selection of a formulation with the duration of action tailored to the needs of the patient. For example, Ritalin-SR, a long-acting methylphenidate, produces sustained release of medication for about 8 hours, whereas Concerta, another methylphenidate, provides immediate and delayed-release action for about 12 hours of action.

Ritalin is the most widely prescribed stimulant for ADHD, but Dexedrine (dextroamphetamine) is equally effective. Immediate-release Ritalin is short acting and begins to work in 30–60 minutes after administration, with duration of 2–5 hours. The advantage is that it works quickly, but the duration of action is short and requires dosing two or three times a day. Similarly, Dexedrine is a short-acting stimulant with peak effects 1–2 hours after administration, and the effects last 2–5 hours.

Because multiple dosing may be difficult for patients, especially school-age children, Ritalin and Dexedrine come in long-acting preparations that provide 6–8 hours of benefit from a single morning dose. The long-acting preparations of Ritalin and Dexedrine provide flexible dosing options, but the formulations of stimulants are made confusing by their different designations: for Ritalin, "SR" denotes *sustained-release* and "LA" denotes *long-acting;* for Metadate, "ER" denotes *extended-release* and "CD" denotes *controlled-delivery;* for Adderall, "XR" denotes *extended-release;* and for Dexedrine, the "Spansule" is a trademark for a *long-acting* capsule form.

Adderall is mixture of dextroamphetamine and amphetamine, and Adderall XR is the extended-release preparation of the mixture. Adderall provides about 5 hours of effect, whereas Adderall XR extends the duration to 8–10 hours.

With recent advances in drug delivery systems, manufacturers have incorporated new technology in the formulation of stimulants to provide a bimodal action from a single tablet or capsule. This bimodal delivery system can release 20%–50% of the medication immediately and the remainder in the 10–12 hours following. For example, Concerta (methylphenidate) uses a system that provides immediate and extended delivery of medication. It releases about 22% of the medication within 1–2 hours and the remainder of the drug over 10–12 hours. Similarly, Adderall XR, Metadate CD, and Ritalin LA use this bimodal delivery system. The advantage of this preparation is that it provides immediate effect from a single morning dose and extended action into the evening, but by bedtime the effects of the medication wear off without affecting sleep. The different preparations of amphetamine and methylphenidate are summarized in the table on the next two pages.

| Brand name | Generic name | Available strengths | Dosing frequency (approximate duration of action) |
|---|---|---|---|
| | | **STIMULANTS** | |
| **Amphetamines** | | | |
| *Short-acting* | | | |
| DextroStat | Dextroamphetamine (immediate release) | 5, 10 mg tablets | Two to three times a day (4–6 hours) |
| Liquadd | Dextroamphetamine oral solution | 5 mg/5 mL | |
| Adderall | Amphetamine mixture (immediate release) | 5, 7.5, 10, 12.5, 15, 20, 30 mg tablets | Two times a day (4–6 hours) |
| *Long-acting* | | | |
| Dexedrine Spansules | Dextroamphetamine (sustained release) | 5, 10, 15 mg capsules | Once a day in the morning (6–8 hours) |
| Adderall XR | Amphetamine mixture (extended release) | 5, 10, 15, 20, 25, 30 mg capsules | Once a day in the morning (8–10 hours) |
| Vyvanse | Lisdexamfetamine | 20, 30, 40, 50, 60, 70 mg capsules | Once a day in the morning (up to 12 hours) |
| **Methylphenidates** | | | |
| *Short-acting* | | | |
| Ritalin | Methylphenidate | 5, 10, 20 mg tablets | Two to three times a day (2–5 hours) |
| Methylin | Methylphenidate | 2.5, 5, 10 mg chewable tablets | Two to three times a day (3–5 hours) |
| Methylin Oral Solution | Methylphenidate | 5 mg/5 mL, 10 mg/5 mL | Two to three times a day (3–5 hours) |
| *Intermediate-acting* | | | |
| Ritalin-SR | Methylphenidate (sustained release) | 20 mg tablet | Once a day (6–8 hours) |
| Methylin ER | Methylphenidate (extended release) | 10, 20 mg tablets | One to two times a day (6–8 hours) |
| Metadate ER | Methylphenidate (extended release) | 10, 20 mg tablets | One to two times a day (6–8 hours) |
| *Long-acting* | | | |
| Ritalin LA | Methylphenidate (extended release) | 10, 20, 30, 40 mg capsules | Once a day in the morning (8–10 hours) |
| Metadate CD | Methylphenidate (extended release) | 10, 20, 30, 40, 50, 60 mg capsules | Once a day in the morning (8–10 hours) |

| Brand name | Generic name | Available strengths | Dosing frequency (approximate duration of action) |
|---|---|---|---|
| | | **STIMULANTS** *(continued)* | |
| **Methylphenidates** *(continued)* | | | |
| *Long-acting (continued)* | | | |
| Concerta | Methylphenidate (extended release) | 18, 27, 36, 54 mg tablets | Once a day in the morning (8–12 hours) |
| Daytrana | Methylphenidate (topical patch) | 10, 15, 20, 30 mg patch | Once a day in the morning (9 hours/day, off 15 hours) |
| **Dexmethylphenidate** | | | |
| Focalin | Dexmethylphenidate (immediate action) | 2.5, 5, 10 mg tablets | Two times a day (2–5 hours) |
| Focalin XR | Dexmethylphenidate (delayed action) | 5, 10, 15, 20 mg capsules | Once a day (5–8 hours) |
| | | **NONSTIMULANTS** | |
| Catapres | Clonidine* | 0.1, 0.2, 0.3 mg tablets | Once a day |
| Tenex | Guanfacine* | 1, 2 mg tablets | Once a day |
| Strattera | Atomoxetine | 10, 18, 25, 40, 60, 80, 100 mg capsules | Once a day in the morning (24 hours) |

*Off-label use for attention-deficit/hyperactivity disorder (ADHD).

## Common Side Effects

The common side effects associated with stimulants are rapid heart rate, palpitations, restlessness, insomnia, dry mouth, constipation, nausea, diarrhea, loss of appetite, weight loss, and elevation of blood pressure. (See individual handouts for common side effects of nonstimulants.)

## Adverse Reactions and Precautions

Stimulants, particularly the amphetamines, have a high potential for abuse. Individuals with a history of alcohol and substance abuse may be at risk for abusing stimulants. Individuals who abuse stimulants develop tolerance and psychological dependence that may result in addiction. With long-term abuse of stimulants and the resulting sleepless nights, the individual may develop psychotic symptoms.

Stimulants may increase blood pressure. Individuals with a history of high blood pressure or heart disease should be cautious about taking stimulants because these agents can exacerbate these conditions. Uncontrolled high blood pressure can have serious consequences, including stroke and heart attacks. Patients taking stimulants should routinely check their blood pressure.

Individuals with a history of seizure disorder should be cautious while taking stimulants because these agents can lower the seizure threshold.

In children and adolescents who are still in their growth period, stimulants can suppress linear growth. Physicians commonly interrupt treatment, if possible, on weekends and holidays, when children are not in school, for growth catch-up. Children and adolescents taking stimulants require close monitoring for growth suppression and periodic measuring of their height. This effect is not a concern in the adult population.

Stimulants may make tics worse in individuals with a tic disorder (i.e., twitching of a muscle group, especially in the face).

Stimulants should be avoided, or used with caution, by patients with a diagnosis of schizophrenia or bipolar disorder. Stimulants are frequently abused in this population, and high doses of stimulants may trigger psychosis and mania.

## Use in Pregnancy and Breastfeeding: Pregnancy Category C

The stimulants have not been tested in women to determine their safety in pregnancy. The effects of these medications on the developing fetus in pregnant women are unknown. Women who are pregnant or may become pregnant should discuss this with their physician.

Nursing mothers should not take any stimulant, because small amounts will pass into breast milk and be ingested by the baby. If stopping the stimulant is not an alternative, breastfeeding should not be started or should be discontinued.

## Possible Drug Interactions

Stimulants should not be taken in combination with a group of antidepressants known as **monoamine oxidase inhibitors** (MAOIs). The combination may precipitate increases in blood pressure. This and other significant drug interactions reported with stimulants are summarized in the table below.

| | |
|---|---|
| Monoamine oxidase inhibitors (MAOIs) (e.g., Parnate, Emsam, Nardil, Marplan) | MAOIs should not be taken with methylphenidates (e.g., Concerta, Ritalin, Focalin), dextroamphetamines (e.g., DextroStat, Adderall, Adderall XR), and Strattera. The combination may precipitate dangerous elevation of blood pressure. |
| Weight-loss medications (e.g., Meridia) | Weight-loss medications, prescription and nonprescription, should not be taken with dextroamphetamines/amphetamines or methylphenidates. The combination may increase blood pressure or cause irritability, insomnia, and other adverse reactions from excessive stimulation. |
| Coumadin (warfarin) | Methylphenidate may increase the anticoagulant action of Coumadin. |
| Prozac (fluoxetine), Paxil (paroxetine), Tagamet (cimetidine), Wellbutrin (bupropion), and Norvir (ritonavir) | These medications may inhibit the metabolism of Strattera and should be monitored closely when used together. |

## Overdose

The severity of acute amphetamine and methylphenidate overdose depends on the amount ingested. The individual may experience a progression of the following symptoms from an acute overdose: restlessness, agitation, irritability, insomnia, hyperactivity, confusion, elevated blood pressure, rapid heart rate, delirium, hallucinations, irregular heartbeat, convulsions, coma, circulatory collapse, and death.

Any suspected overdose should be treated as an emergency. The person should be taken to the emergency room for observation and treatment. The prescription bottle of medication (and any other medication suspected in the overdose) should be brought as well, because the information on the prescription label can be helpful to the treating physician in determining the number of pills ingested.

## Special Considerations

- Dexedrine and Ritalin should be taken early in the morning, especially the sustained-release preparations, so the action of the medication does not extend into bedtime hours and interfere with sleep.
- Do not chew or crush the sustained-release or long-acting preparations; swallow the tablet or capsule whole.
- Do not take more than instructed by your physician.
- If the stimulant causes pronounced nervousness, restlessness, insomnia, loss of appetite, or weight loss, notify your physician.
- If you miss a dose, take it as soon as possible. If it is close to the next scheduled dose, skip the missed dose and continue on your regular dosing schedule. Do not take double doses.
- Store the medication in its originally labeled, light-resistant container, away from heat and moisture. Heat and moisture may precipitate breakdown of your medication, and the medication may lose its therapeutic effects.
- Keep your medications out of reach of children.

***If you have any questions about your medication, consult your physician or pharmacist.***

## Notes



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