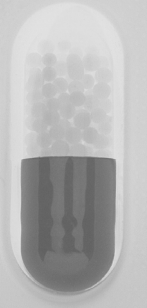


Stimulants



Adderall and Adderall-XR (amphetamine mixtures)
Concerta (methylphenidate, controlled release)
Dexedrine, Dexedrine Spansules (dextroamphetamine)
Focalin (dexmethylphenidate)
Metadate, Metadate-ER, and Metadate-CD
(methylphenidate, extended release)
Ritalin, Ritalin-SR, Ritalin-LA (methylphenidate)
Strattera (atomoxetine)

The psychostimulants, or 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.

The use of a medication for its approved indication 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 these medications for these unapproved indications. One unlabeled use of stimulants is for augmentation of antidepressants in treating refractory depression. For patients with chronic treatment-resistant depression, for example, stimulants in combination with antidepressants can provide symptomatic relief and improvement beyond that experienced with antidepressants alone.

In numerous clinical studies and decades of clinical experience, 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.

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 (methylphenidate)**, 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 8–12 hours of benefit from a single morning dose. The long-acting preparations of Ritalin and Dexedrine provide flexible dosing options, but these formulations 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” is for *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 about 8 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 the first hour and the remainder of the drug over 10–12 hours. Similarly, Metadate-CD, Ritalin-LA, and Adderall-XR 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 below.

Brand name	Generic name	Available strengths	Dosing frequency (approximate duration of action)
Amphetamines			
Dexedrine	Dextroamphetamine (immediate release)	5, 10 mg tablets	Two to three times a day (3–5 hours)
Dexedrine Spansules	Dextroamphetamine (sustained release)	5, 10, 15 mg capsules	Once a day in the morning (8–12 hours)
Adderall	Amphetamine/dextroamphetamine mixture (immediate release)	5, 7.5, 10, 12.5, 15, 20, 30 mg tablets	Two times a day (4–6 hours)
Adderall-XR	Amphetamine/dextroamphetamine mixture (extended release)	5, 10, 15, 20, 25, 30 mg capsules	Once a day in the morning (12 hours)
Methylphenidates			
Ritalin	Methylphenidate (immediate release)	5, 10, 20 mg tablets 2.5, 5, 10 mg chewable tablets	Two or three times a day (3–5 hours)
Ritalin-SR	Methylphenidate (sustained release)	20 mg	Once a day in the morning (8–10 hours)

(continued)

Brand name	Generic name	Available strengths	Dosing frequency (approximate duration of action)
Methylphenidates (<i>continued</i>)			
Ritalin-LA	Methylphenidate (long acting)	20, 30, 40 mg capsules	Once a day in the morning (12 hours)
Metadate-CD	Methylphenidate (controlled release)	20 mg capsule	Once a day in the morning (12 hours)
Concerta	Methylphenidate (extended release)	18, 27, 36, 54 mg caplets	Once a day in the morning (12 hours)
Focalin	Dexmethylphenidate	2.5, 5, 10 mg tablets	Two times daily (4–6 hours)
Selective norepinephrine reuptake inhibitor			
Strattera	Atomoxetine	10, 18, 25, 40, 60 mg capsules	One or two times a day (5 hours)

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.

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.

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.

Ismelin (guanethidine)	The antihypertensive effects of Ismelin (i.e., lowering of blood pressure) may be decreased when combined with amphetamines or methylphenidate.
Monoamine oxidase inhibitors (MAOIs)	MAOI antidepressants (e.g., Parnate) should not be taken with amphetamines and methylphenidate; the combination may precipitate dangerous elevation of blood pressure.
Selective serotonin reuptake inhibitors (SSRIs)	Ritalin and other methylphenidates may elevate the blood levels of SSRI antidepressants (e.g., Paxil, Prozac) and enhance their effects.
Weight-loss medications	Weight-loss medications, prescription and non-prescription, should not be taken with stimulants. Excess stimulation may cause agitation, irritability, insomnia, and other adverse reactions.

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.

Overdose

The severity of acute amphetamine and methylphenidate overdose depends on the amount ingested. An 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 heart beat, convulsions, coma, circulatory collapse, and death.

Any suspected overdose should be treated as an emergency. The person should be taken to the emergency department 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.

