STIMULANT C-II

Mixed Amphetamine Salts

Adderall, Adderall XR, Mydayis

A 3:1 blend of dextro- and levoamphetamine salts; the most widely prescribed amphetamine product for ADHD in the United States.

USUAL ADULT RANGE	HALF-LIFE	METABOLISM	ONSET
IR 10-40 mg/d; XR 20-30 mg/d	d 9-11 h; l 11-14 h	CYP2D6, deamination; renal	30-60 min; IR lasts 4-6 h

FDA BOXED WARNING

Abuse, misuse, addiction, and dependence: mixed amphetamine salts have a high potential for abuse and misuse that can lead to substance use disorder including addiction; misuse at high doses or by snorting or injection can result in overdose and death. Assess risk before prescribing and monitor throughout treatment.

INDICATIONS

- FDA-approved for attention-deficit/hyperactivity disorder; immediate-release tablets are labeled from age 3 and Adderall XR from age 6 years.
- Mydayis, the triple-bead extended-release capsule, is approved for ADHD in patients age 13 years and older with about 16 hours of coverage.
- Immediate-release mixed amphetamine salts are FDA-approved for narcolepsy in patients age 6 years and older.
- Used off-label for treatment-resistant depression augmentation and for apathy or fatigue in medically ill, cancer, or geriatric patients.
- Used off-label for binge eating disorder, where lisdexamfetamine rather than mixed salts holds the actual FDA indication.
- Chosen over methylphenidate when a longer duration or a stronger dopamine-releasing effect is wanted, since the classes are not interchangeable.

DOSING & TITRATION

- Immediate-release for ADHD in patients 6 and older: start **5 mg** PO once or twice daily, increase by **5 mg/day** weekly, usual max **40 mg/day**.
- Adderall XR: children 6-12 start **5-10 mg** each morning to a maximum of **30 mg/day**; adults typically use **20 mg** once daily in the morning.
- Mydayis: adults start **12.5-25 mg** each morning with a maximum of **50 mg/day**; patients 13-17 years should not exceed 25 mg/day.
- Give the last immediate-release dose by early afternoon and Mydayis on waking, since late dosing is the usual cause of treatment-emergent insomnia.
- Extended-release capsules may be opened onto applesauce and swallowed without chewing; do not divide the contents of a single capsule across doses.
- No taper is pharmacologically required, but abrupt cessation after high chronic doses produces crash fatigue, hypersomnia, and dysphoria.

MECHANISM OF ACTION

- Acts as a substrate at the dopamine and norepinephrine transporters, reversing transporter flux so catecholamines are pushed out into the synapse.
- Blocks vesicular monoamine transporter 2 packaging and inhibits monoamine oxidase weakly, raising the cytoplasmic pool available for release.
- Release is not activity-dependent, which explains greater potency and higher abuse liability than the methylphenidate class.
- The dextro isomer favors dopaminergic effects while the levo isomer is relatively more noradrenergic, giving a mixed clinical profile.
- Increased prefrontal catecholamine tone improves working memory and impulse control, while striatal effects drive both benefit and reinforcement.

PHARMACOKINETICS

- Immediate-release Tmax is about 3 hours; Adderall XR is bimodal with a second bead release near 7 hours and Mydayis adds a third pulse.
- Half-life is roughly 9-11 hours for d-amphetamine and 11-14 hours for l-amphetamine in adults, and shorter in children.
- Partly metabolized by CYP2D6 to 4-hydroxyamphetamine and by deamination, but a large fraction is excreted unchanged in urine.
- Renal elimination is strongly pH dependent: alkaline urine slows excretion and raises levels, while acidic urine shortens duration.
- Food delays Tmax of the extended-release capsules by about 2.5 hours without changing total exposure, so timing consistency matters more than fasting.

ADVERSE EFFECTS

- Anorexia and weight loss, insomnia, dry mouth, headache, irritability, and emotional lability are common and largely dose related.
- Blood pressure rises about 2-5 mmHg and heart rate 3-6 bpm on average, with a minority developing sustained hypertension or palpitations.
- Late-day rebound with irritability or tearfulness is common as levels fall and often responds to a small afternoon immediate-release dose.
- Psychosis or mania can emerge at usual doses in about 0.1 percent of patients, requiring the stimulant to be stopped rather than covered.
- Peripheral vasculopathy including Raynaud phenomenon, priapism, and rare serious cardiovascular events including sudden death are labeled risks.
- Growth suppression in children of roughly 1-2 cm and 1-3 kg over the first years of continuous treatment warrants growth chart tracking.

MONITORING

- Baseline height, weight, pulse, blood pressure, cardiac and family history of sudden death, and screening for tics, psychosis, and substance misuse.
- Repeat pulse, blood pressure, and weight at every visit; plot height at least twice yearly in children on continuous treatment.
- Use a validated ADHD rating scale at baseline and after each titration step and document target symptoms rather than global impressions.
- Assess sleep onset, evening appetite, mood in the late afternoon, and any cardiac symptoms such as exertional chest pain or syncope.
- Review the prescription drug monitoring program at each refill and ask directly about sharing, selling, or nonoral use of the medication.

INTERACTIONS & CAUTIONS

- Contraindicated within 14 days of an MAOI, including phenelzine, tranylcypromine, selegiline, and linezolid, because of hypertensive crisis risk.
- Urinary alkalinizers such as sodium bicarbonate and acetazolamide raise amphetamine levels, while ascorbic acid and acidic urine lower them.
- CYP2D6 inhibitors such as fluoxetine, paroxetine, bupropion, and quinidine raise exposure and increase the risk of serotonin syndrome per the label.
- Additive pressor effects with decongestants, other stimulants, SNRIs, and thyroid hormone; avoid duplicate stimulant therapy without a clear plan.
- Amphetamines can blunt the antihypertensive effect of guanethidine and similar agents and can raise the risk of arrhythmia with halogenated anesthetics.

SPECIAL POPULATIONS

- Pregnancy: associated with lower birth weight and preterm birth in observational data; use only when benefit clearly outweighs risk and document the discussion.
- Lactation: amphetamine concentrates in breast milk with a relative infant dose of about 2-14 percent, so monitor the infant for irritability and poor feeding.
- Pediatric: immediate-release is labeled from age 3, but treatment before age 6 is rarely appropriate before behavioral parent training is tried.
- Geriatric: reduce starting dose, avoid in uncontrolled hypertension or recent cardiac events, and watch for insomnia, delirium, and appetite loss.
- Renal impairment: clearance falls, so cap doses in severe impairment and avoid in end-stage renal disease, where amphetamines are not dialyzable.

PRESCRIBING PEARLS

- Amphetamines are roughly twice as potent per milligram as methylphenidate; do not convert doses one for one.
- Rebound at 4 pm usually needs a small immediate-release booster, not a bigger morning dose.
- Baking soda, antacids, and alkaline urine prolong the dose; acidic drinks shorten it.

References

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NOTE

References follow APA 7th edition style. Dosing, boxed warnings, and interaction data change; confirm every clinical decision against the current FDA prescribing information (DailyMed) and your institution's formulary. This sheet is an educational quick reference and does not replace the full label or clinical judgment.