STIMULANT C-II

Dextroamphetamine

Dexedrine Spansule, Zenzedi, ProCentra, Xelstrym (transdermal)

The single d-isomer amphetamine, useful when mixed salts are poorly tolerated or when a simple, cheap immediate-release option is needed.

USUAL ADULT RANGE	HALF-LIFE	METABOLISM	ONSET
5-40 mg/day PO divided	10-12 h adults; ~9 h children	CYP2D6, deamination; renal	30-60 min; IR lasts 4-6 h

⚠ FDA BOXED WARNING

Abuse, misuse, addiction, and dependence: dextroamphetamine has 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, with immediate-release tablets labeled from age 3 and Spansule capsules from age 6.
- FDA-approved for narcolepsy in patients age 6 years and older, typically at 5-60 mg/day in divided doses titrated to symptom control.
- Xelstrym transdermal system is approved for ADHD in patients age 6 and older and is the only amphetamine patch on the US market.
- Preferred over mixed salts by some prescribers when the levo isomer appears to drive jitteriness, irritability, or cardiovascular effects.
- Used off-label for treatment-resistant depression augmentation and for apathy or fatigue in palliative care and medically ill adults.
- Used off-label for idiopathic hypersomnia and residual sleepiness in treated obstructive sleep apnea when modafinil is ineffective.

DOSING & TITRATION

- ADHD in patients 6 and older: start **5 mg** PO once or twice daily, increase by **5 mg/day** at weekly intervals; doses above **40 mg/day** are rarely useful.
- Children 3-5 years: start **2.5 mg** PO daily and increase by 2.5 mg/day weekly, recognizing that drug treatment at this age is a second-line step.
- Dexedrine Spansule: **5-30 mg** PO once daily in the morning, replacing divided immediate-release dosing when a smoother curve is wanted.
- Narcolepsy: **5-60 mg/day** PO in divided doses; give the first dose on waking and additional doses at 4-6 hour intervals.
- Xelstrym: start **9 mg/9 h** applied to hip, upper arm, chest, upper back, or flank 2 hours before effect is needed; maximum 18 mg per 9 hours.
- No taper is required, though stopping high chronic doses abruptly causes fatigue, hypersomnia, hyperphagia, and depressed mood for several days.

MECHANISM OF ACTION

- Enters presynaptic terminals through the dopamine and norepinephrine transporters and reverses their direction, releasing stored catecholamines.
- Disrupts vesicular monoamine transporter 2 storage, moving monoamines into the cytoplasm where they become available for carrier-mediated efflux.
- Weak monoamine oxidase inhibition further raises cytoplasmic catecholamine concentration and prolongs the released signal.
- Contains only the dextro isomer, which is more dopaminergic and roughly twice as potent as the levo isomer at central sites.
- The resulting prefrontal catecholamine surge improves attention and impulse control, while nucleus accumbens effects create reinforcement risk.

PHARMACOKINETICS

- Immediate-release Tmax is about 3 hours and Spansule Tmax about 8 hours, giving roughly 4-6 and 8 hours of clinical coverage respectively.
- Elimination half-life is 10-12 hours in adults and closer to 9 hours in children, so twice-daily immediate-release dosing is typical.
- Metabolized by CYP2D6 to 4-hydroxyamphetamine and by side-chain deamination, with a substantial fraction excreted unchanged in urine.
- Excretion is highly pH dependent: alkaline urine prolongs the half-life sharply while acidification can shorten it to as little as 7 hours.
- The Xelstrym patch avoids first-pass effects and delivers steadily over a 9-hour wear time, with effect declining over 2 hours after removal.

ADVERSE EFFECTS

- Appetite suppression, weight loss, insomnia, dry mouth, headache, and irritability are the dominant dose-limiting effects in practice.
- Blood pressure and heart rate rise modestly, but new hypertension, palpitations, or exertional chest pain require reassessment or discontinuation.
- Emotional blunting, anxiety, and end-of-dose rebound irritability are common complaints that often reflect dose or timing rather than nonresponse.
- Psychosis, mania, aggression, or new tics can emerge at usual doses and are indications to stop the stimulant rather than to add treatment.
- Peripheral vasculopathy including Raynaud phenomenon, priapism in males, and rare sudden cardiac death in structural heart disease are labeled risks.
- Xelstrym adds application-site reactions and permanent skin hypopigmentation at the site, which is a labeled dermatologic warning.

MONITORING

- Baseline weight, height, blood pressure, pulse, cardiac and family sudden-death history, and screening for psychosis, tics, and substance misuse.
- Recheck pulse, blood pressure, and weight each visit, plotting growth at least every 6 months in children on continuous treatment.
- Use validated ADHD or sleepiness scales such as ADHD-RS-5 or the Epworth scale at baseline and after every dose change.
- Screen for insomnia, evening rebound, and appetite pattern, which usually direct formulation and dosing time more than dose size.
- Check the prescription drug monitoring program at each refill and ask directly about diversion, nonoral use, and early refill requests.

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 levels, and acidifying agents including ascorbic acid lower them.
- CYP2D6 inhibitors such as fluoxetine, paroxetine, bupropion, and quinidine raise amphetamine exposure and per the label add serotonin syndrome risk.
- Additive cardiovascular effects with decongestants, thyroid hormone, other stimulants, and SNRIs; avoid stacking stimulants without a clear plan.
- Amphetamines antagonize guanethidine-type antihypertensives and can precipitate arrhythmia when combined with halogenated general anesthetics.

SPECIAL POPULATIONS

- Pregnancy: observational data link amphetamine use to lower birth weight and preterm birth; use only when the benefit clearly outweighs the risk.
- Lactation: dextroamphetamine concentrates in breast milk with a relative infant dose near 2-14 percent, so watch for infant irritability and poor feeding.
- Pediatric: labeled from age 3, but behavioral parent training should precede medication in preschoolers and doses must be weight-appropriate.
- Geriatric: use the lowest effective dose, avoid in uncontrolled hypertension or recent myocardial infarction, and watch for delirium and weight loss.
- Renal impairment: clearance falls with declining eGFR, so cap the dose in severe impairment and avoid use in end-stage renal disease.

☆ PRESCRIBING PEARLS

- Alkaline urine can double amphetamine exposure; ask about bicarbonate, antacids, and acetazolamide.
- One Spansule often replaces twice-daily immediate-release dosing with less midday rebound.
- Xelstrym can leave permanent skin lightening at the site; rotate sites and warn patients up front.

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.