STIMULANT C-II

Lisdexamfetamine

Vyvanse, Vyvanse Chewable

An inactive lysine-amphetamine prodrug activated by red blood cells, giving smooth all-day coverage and lower intranasal abuse appeal.

USUAL ADULT RANGE	HALF-LIFE	METABOLISM	ONSET
30-70 mg/day PO once daily	prodrug <1 h; d-amph ~11 h	RBC hydrolysis, not CYP	1.5-2 h; lasts 13-14 h

FDA BOXED WARNING

Abuse, misuse, addiction, and dependence: lisdexamfetamine 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 in children age 6 years and older, adolescents, and adults as a once-daily morning dose.
- FDA-approved for moderate to severe binge eating disorder in adults, the only stimulant with this indication, based on binge-day reduction trials.
- Explicitly not approved and not recommended for weight loss or obesity, a limitation stated in the label and often ignored in practice.
- Favored when abuse or diversion risk is a concern, since the prodrug must be hydrolyzed systemically and is not activated by snorting or injection.
- Used off-label for treatment-resistant depression augmentation and for cognitive fatigue in medically ill or post-traumatic brain injury patients.
- Chewable tablets and dispersible capsule contents make it useful off-label as a stimulant option for patients who cannot swallow capsules.

DOSING & TITRATION

- ADHD: start **30 mg** PO each morning, increase by **10-20 mg** at weekly intervals to a maximum of **70 mg/day**; give as a single morning dose.
- Binge eating disorder in adults: start **30 mg** each morning, titrate by 20 mg weekly to the target range of **50-70 mg/day**, maximum 70 mg/day.
- Renal impairment: maximum **50 mg/day** when eGFR is 15 to under 30 mL/min/1.73 m2 and **30 mg/day** in end-stage disease; not removed by dialysis.
- Capsule contents may be emptied into water, orange juice, or yogurt and consumed immediately; a single capsule must not be split between doses.
- Chewable tablets are milligram-equivalent to capsules and must be chewed completely before swallowing with adequate fluid.
- No taper is required pharmacologically, but abrupt withdrawal after chronic high doses causes fatigue, hypersomnia, and dysphoria for several days.

MECHANISM OF ACTION

- The lysine conjugate is pharmacologically inert until peptide bond hydrolysis in red blood cells releases active d-amphetamine.
- Released d-amphetamine reverses dopamine and norepinephrine transporter flux and disrupts vesicular storage, producing sustained catecholamine release.
- Rate-limited enzymatic conversion flattens the plasma curve, which reduces euphoria and gives a longer, smoother clinical effect.
- Increased prefrontal norepinephrine and dopamine tone improves sustained attention, working memory, and impulse control.
- In binge eating disorder the benefit is thought to come from dopaminergic effects on reward-driven eating and on impulsivity rather than appetite alone.

PHARMACOKINETICS

- Prodrug Tmax is about 1 hour while d-amphetamine Tmax is roughly 3.5 hours with capsules and 4.4 hours with chewable tablets.
- Prodrug half-life is under 1 hour; the liberated d-amphetamine half-life is about 11-12 hours in adults, supporting once-daily dosing.
- Conversion occurs by hydrolysis in blood rather than by hepatic CYP enzymes, so CYP-based drug interactions are minimal.
- Food does not affect exposure, though a high-fat meal delays Tmax by about an hour; capsules can be dissolved in water, juice, or yogurt.
- Elimination is largely renal as amphetamine and metabolites, and urinary pH shifts alter amphetamine clearance as with other amphetamines.

ADVERSE EFFECTS

- Decreased appetite in about 27 percent, insomnia in 19-27 percent, dry mouth, weight loss, irritability, anxiety, and headache are common.
- Blood pressure and pulse rise modestly, averaging 2-5 mmHg and 3-7 bpm, with occasional clinically important hypertension or tachycardia.
- Late-day dysphoria or rebound is less common than with immediate-release amphetamine but still occurs, especially at higher milligram doses.
- New psychosis, mania, or aggression can develop at usual doses and requires stopping the stimulant rather than adding an antipsychotic.
- Peripheral vasculopathy including Raynaud phenomenon, priapism, and rare sudden cardiac death in structural heart disease are labeled warnings.
- Growth suppression occurs in children, with expected slowing of about 1-2 cm and 1-3 kg over the first years of continuous treatment.

MONITORING

- Baseline height, weight, pulse, blood pressure, cardiac and family sudden-death history, and screening for psychosis, tics, and substance misuse.
- Recheck vital signs and weight at each visit and plot height at least every 6 months in children and adolescents on continuous treatment.
- Track ADHD symptoms with a validated scale, or binge days per week in binge eating disorder, at baseline and after each dose change.
- Reassess renal function periodically in older adults or those on nephrotoxic agents, since dose caps apply below an eGFR of 30.
- Review the prescription drug monitoring program at each refill and ask directly about early refills, sharing, and nonoral use.

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 exposure, while acidifying agents shorten its effect.
- Serotonergic drugs including SSRIs, SNRIs, triptans, and tramadol raise the risk of serotonin syndrome when combined with amphetamines.
- Additive pressor effect with decongestants, thyroid hormone, and other stimulants; avoid duplicate stimulant therapy without a specific plan.
- CYP interactions are minimal because activation depends on red blood cell hydrolysis rather than hepatic oxidation.

SPECIAL POPULATIONS

- Pregnancy: amphetamine exposure is linked to lower birth weight and preterm birth in observational data, so reserve for clear clinical need.
- Lactation: amphetamine concentrates in milk with a relative infant dose near 2-14 percent; monitor the infant for agitation and poor weight gain.
- Pediatric: approved from age 6 for ADHD but not for binge eating disorder, which remains an adult indication only.
- Geriatric: no dedicated studies; start at 30 mg or lower, check blood pressure, and reassess cardiovascular risk before continuing.
- Renal impairment requires the labeled dose caps, whereas no hepatic adjustment is specified since activation is not hepatic.

PRESCRIBING PEARLS

- Onset takes 1.5-2 hours; patients expecting an immediate lift often mislabel it as ineffective.
- It is the only stimulant approved for binge eating disorder, and it is not approved for weight loss.
- Dissolving the capsule in liquid does not speed onset, since red blood cells still gate activation.

References

Cortese, S. (2020). Pharmacologic treatment of attention deficit-hyperactivity disorder. *New England Journal of Medicine, 383*(11), 1050-1056. https://doi.org/10.1056/NEJMra1917069

Cortese, S., Adamo, N., Del Giovane, C., Mohr-Jensen, C., Hayes, A. J., Carucci, S., Atkinson, L. Z., Tessari, L., Banaschewski, T., Coghill, D., Hollis, C., Simonoff, E., Zuddas, A., Barbui, C., Purgato, M., Steinhausen, H. C., Shokraneh, F., Xia, J., & Cipriani, A. (2018). Comparative efficacy and tolerability of medications for attention-deficit hyperactivity disorder in children, adolescents, and adults: A systematic review and network meta-analysis. *The Lancet Psychiatry, 5*(9), 727-738. https://doi.org/10.1016/S2215-0366(18)30269-4

McElroy, S. L., Hudson, J. I., Mitchell, J. E., Wilfley, D., Ferreira-Cornwell, M. C., Gao, J., Wang, J., Whitaker, T., Jonas, J., & Gasior, M. (2015). Efficacy and safety of lisdexamfetamine for treatment of adults with moderate to severe binge-eating disorder: A randomized clinical trial. *JAMA Psychiatry, 72*(3), 235-246. https://doi.org/10.1001/jamapsychiatry.2014.2162

National Institute for Health and Care Excellence. (2018). *Attention deficit hyperactivity disorder: Diagnosis and management* (NICE guideline NG87). https://www.nice.org.uk/guidance/ng87

Stahl, S. M. (2021). *Stahl's essential psychopharmacology: Neuroscientific basis and practical applications* (5th ed.). Cambridge University Press.

Takeda Pharmaceuticals America. (2025). *Vyvanse (lisdexamfetamine dimesylate) capsules and chewable tablets [Prescribing information]*. U.S. Food and Drug Administration. https://dailymed.nlm.nih.gov/dailymed/

Wolraich, M. L., Hagan, J. F., Allan, C., Chan, E., Davison, D., Earls, M., Evans, S. W., Flinn, S. K., Froehlich, T., Frost, J., Holbrook, J. R., Lehmann, C. U., Lessin, H. R., Okechukwu, K., Pierce, K. L., Winner, J. D., & Zurhellen, W. (2019). Clinical practice guideline for the diagnosis, evaluation, and treatment of attention-deficit/hyperactivity disorder in children and adolescents. *Pediatrics, 144*(4), e20192528. https://doi.org/10.1542/peds.2019-2528

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.