Zenzedi

(dextroamphetamine sulfate)

Zenzedi (dextroamphetamine sulfate); CII

Full Prescribing Information	DailyMed Drug Information

Summary

Zenzedi is an immediate-release, short-acting dextroamphetamine tablet approved for narcolepsy and for ADHD in patients aged 3 to 16. It is single-isomer dextroamphetamine, carrying no levoamphetamine and less peripheral noradrenergic load than an equivalent mixed-salt dose. Its differentiator is the age floor: 3 years is the lowest approved age in this library, and the seven-step ladder starting at 2.5 mg is what makes that band dosable. Schedule II; brand and generic.

Forms & Strengths

- **Tablets:** 2.5 mg, 5 mg, 7.5 mg, 10 mg, 15 mg, 20 mg, 30 mg
- **Scoring:** the 5 mg tablet is scored, the 10 mg tablet double scored

Dosing

- **Age:**
  - ADHD: 3-16 y/o, the lowest approved age here. Not recommended under 3
  - Narcolepsy: no age bound stated; dose ladder given from age 6
- **Onset:** 30-60 min
- **Duration:** 4-6 hours, the label's own redosing interval
- **Initial Dose:**
  - ADHD, 3-5 y/o: 2.5 mg daily
  - ADHD, 6-16 y/o: 5 mg once or twice daily
  - Narcolepsy, 6-11 y/o: 5 mg daily
  - Narcolepsy, ≥ 12 y/o: 10 mg daily

- **Titration:**
  - ADHD, 3-5 y/o: 2.5 mg at weekly intervals until optimal response
  - ADHD, 6-16 y/o: 5 mg at weekly intervals until optimal response
  - Narcolepsy, 6-11 y/o: 5 mg at weekly intervals
  - Narcolepsy, ≥ 12 y/o: 10 mg at weekly intervals
- **Max Dose:**
  - ADHD, 6-16 y/o: 40 mg/day; only in rare cases will it be necessary to exceed this
  - ADHD, 3-5 y/o: no maximum stated in this label. Titrate to optimal response; 40 mg/day is not transferable downward to a preschooler
  - Narcolepsy: usual range 5-60 mg/day in divided doses
- **Considerations:** First dose on waking, one or two further doses at 4 to 6 hour intervals; avoid late evening doses. The label directs interrupting treatment occasionally to test continued need.

Pharmacology

- **Mechanism:** Blocks reuptake at DAT and NET and promotes presynaptic catecholamine release via VMAT2 and TAAR1; the release component distinguishes amphetamines from methylphenidate
- **Delivery / Release:** Immediate release. Cmax 36.6 ng/mL at about 3 hours, against 23.5 ng/mL at 8 hours for the SR capsule
- **Formulation:** Single-isomer dextroamphetamine sulfate; no levoamphetamine
- **Metabolism:** CYP2D6 to 4-hydroxyamphetamine. Half-life about 12 hours; the shorter duration is the peak-and-fall profile, not faster clearance
- **Pharmacogenomics:** No genotype-directed dosing in the label; the actionable consequence is the CYP2D6-inhibitor interaction
- **Class Positioning:** A higher earlier peak than Dexedrine Spansule, a finer ladder, and the 3 to 5 year band it lacks. Single-isomer where IR Adderall is mixed salts

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Indications

- **Narcolepsy** (ICD-10: G47.419): no age bound stated; dosing from age 6
- **ADHD** (ICD-10: F90.0, F90.1, F90.2, F90.8, F90.9): patients 3 to 16 y/o, within a total treatment program

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Off-Label Uses

- **Preschool ADHD, where approval and guideline diverge** (ICD-10: F90.x): FDA approves from age 3; evidence for amphetamine in preschoolers is limited.

- AAP places behavioral parent training first-line at 4 to under 6 (grade A) and names methylphenidate, not amphetamine, if medication is added (AAP 2019).
- **ADHD at 17 and older** (ICD-10: F90.x): this label stops at 16; switch to a product with an adult indication.
- **Binge eating disorder** (ICD-10: F50.81): lisdexamfetamine holds it, adults only; insufficient here.
- **Where the evidence does not support use:** depression augmentation; no pediatric evidence for IR dextroamphetamine (AHRQ 2024).
- **Cognitive enhancement without ADHD:** not an indication.

Contraindications & Warnings

- **Boxed Warning:** Abuse, misuse, and addiction; misuse can cause overdose and death. Assess abuse risk and monitor throughout.
- **Contraindicated:**
  - Known hypersensitivity to amphetamine products
  - MAOI use, current or within 14 days
- **Use with caution** (label Warnings, not contraindications):
  - Structural cardiac abnormality or serious arrhythmia; the label says avoid
  - Pre-existing hypertension; blood pressure and heart rate rise
  - Psychosis or bipolar disorder
  - Prior seizure or EEG abnormality
  - Peripheral vasculopathy including Raynaud phenomenon
  - Tics or Tourette syndrome, personal or family
  - Substance use disorder, patient or household
  - The 3 to 5 year band: no maximum stated, long-term pediatric effects not established. Hold at the lowest effective dose
- **Screen before starting:**
  - Cardiac and family history of sudden death; ECG only if positive
  - Tics and Tourette syndrome, in child and family
  - Mania risk factors, including family history
  - Household abuse and diversion risk
  - Baseline height, weight, blood pressure and heart rate
  - Whether behavioral treatment has been tried, for any child under 6 (AAP 2019)

Drug Interactions

- **MAOIs** (phenelzine, tranylcypromine, selegiline, linezolid): hypertensive crisis and malignant hyperpyrexia, sometimes fatal. Do not give within 14 days.
- **Serotonergic agents** (SSRIs, SNRIs, TCAs, triptans, fentanyl, lithium, tramadol): serotonin syndrome; counsel on symptoms and stop both if it occurs.

- **CYP2D6 inhibitors** (paroxetine, fluoxetine, quinidine, ritonavir): raise exposure; start lower.
- **Alkalinizing agents** (sodium bicarbonate, acetazolamide): raise absorption and reduce excretion; avoid or reduce the dose.
- **Acidifying agents** (ascorbic acid, fruit juices, methenamine): lower absorption and raise excretion; adjust on response.
- **Tricyclics** (desipramine, protriptyline): sustained rise in brain d-amphetamine; monitor.
- **Antiepileptics** (phenytoin, phenobarbital, ethosuximide): delayed absorption; separate dosing, check levels after a stimulant change.
- **Antihypertensives and antihistamines:** effects antagonised; recheck blood pressure, and do not rely on an antihistamine for sleep.
- **Chlorpromazine and haloperidol:** inhibit the stimulant effect; expect loss of benefit.

Administration

- First dose on waking, further doses at 4 to 6 hour intervals.
- Avoid late evening doses; a third dose in a young child costs sleep.
- Splitting a scored tablet is legitimate for an intermediate dose where 2.5 mg is not stocked.
- Prescribe at the lowest effective dosage.
- Interrupt treatment occasionally to see whether therapy is still needed; this label makes that explicit.
- If a dose is missed, skip it; do not double up.
- Store securely, preferably locked, in a child-resistant container.

Side Effects

- **Common:** loss of appetite, weight loss, insomnia, overstimulation, restlessness, dry mouth, headache, dizziness, tremor, dysphoria, palpitations, raised blood pressure
- **Serious:**
  - Sudden death with structural cardiac disease. Investigate exertional chest pain or syncope.
  - Psychotic episodes at recommended doses (rare), mania and new aggression. Consider discontinuing.
  - Serotonin syndrome. Stop both drugs and treat supportively.
  - Seizures. Discontinue.
  - Peripheral vasculopathy with digital ulceration. Reduce or stop.
  - Growth suppression. Interrupt if height or weight gain falls behind.
  - New or worsening motor and verbal tics. Discontinue if clinically appropriate.
  - Prolonged erections; painful erection beyond a few hours is a surgical emergency.

Monitoring & Labs

- **Cardiovascular:** heart rate and blood pressure at baseline, each dose change, and every 6 months.
- **Growth, 6 to 16 y/o:** height, weight and BMI charted at baseline and every 6 months; interrupt if two percentile lines are crossed.
- **Growth, 3 to 5 y/o:** height, weight and BMI at baseline and every 3 months; with no dose ceiling here, growth is the ceiling.
- **Appetite and Sleep:** at every visit and dose change; ask when the last dose is given.
- **Psychiatric and tics:** psychosis, mania, aggression and new tics at every visit.
- **Peripheral vasculopathy:** inspect fingers and toes at every visit.
- **Continued need:** schedule a deliberate interruption at least annually, per this label.
- **Abuse and Diversion:** adherence, pill counts and PDMP check at every refill.
- **Age boundary:** review the indication at the 17th birthday. No routine labs.

Discontinuation & Taper

- May be stopped abruptly at therapeutic doses; no taper is required.
- Withdrawal after abrupt stop following prolonged use: dysphoria, fatigue, vivid dreams, increased appetite.
- Rebound at 4 to 6 hours is offset, not withdrawal; the family may be describing the gap between doses.
- **Planned interruption is a labelled instruction here:** stop occasionally to test whether symptoms recur at a level requiring continued therapy.
- Interrupt treatment where growth or weight gain falls behind.

Pregnancy & Lactation

- **Pregnancy:** No adequate controlled studies; animal teratogenicity only far above human doses. Amphetamine-dependent mothers have more premature delivery and low birth weight. Use only if benefit justifies fetal risk.
- **Lactation:** Label advises against nursing. LactMed: infant dose about 5.7% of the maternal weight-adjusted dose, all four infants studied growing normally. (LactMed 2025)
- **Milk supply:** Dose-related prolactin suppression up to 40% may impair production before lactation is established. (LactMed 2025)
- **Exposure Registry:** None on this label; the National Pregnancy Registry for Psychostimulants (1-866-961-2388) takes amphetamine exposures.

Counseling Points

- **Counsel the family on:**
  - The 4 to 6 hour window and the need for a second, sometimes third, dose.
  - For a preschooler: AAP puts behavioral parent training first and names a different class at that age.
  - For a preschooler: no maximum dose is set, so the growth chart is the ceiling, checked every three months.
  - The 2.5 mg tablet has only one generic supplier; if the pharmacy cannot fill it, split a scored 5 mg tablet.
  - The planned yearly interruption, so it is not heard later as doubt about the diagnosis.
  - Vitamin C and fruit juice can mimic treatment failure; bicarbonate and antacids raise levels.
  - Moving the largest meal to breakfast and to the evening.
  - Locked storage and the child-resistant container.
- **Advise them to call for:**
  - Chest pain on exertion, fainting, or a racing heart that does not settle.
  - New hallucinations, or a young child describing things that are not there.
  - Numbness, coldness or colour change in the fingers or toes.
  - A new or markedly worse tic, or a seizure of any kind.
  - Weight loss, or shoes still fitting after several months.
  - A painful erection lasting more than a few hours.
  - Agitation, shivering, sweating or confusion after an antidepressant change.

References

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Revision #23
Created 2024-12-21 13:55:19 UTC by Josh LeJeune NP
Updated 2026-08-20 06:40:58 UTC by Josh LeJeune NP