Azstarys

(serdexmethylphenidate and dexmethylphenidate)

Azstarys (serdexmethylphenidate and dexmethylphenidate); CII

Full Prescribing Information	DailyMed Drug Information

Summary

Azstarys is a once-daily, long-acting capsule containing dexmethylphenidate together with serdexmethylphenidate, a prodrug converted to dexmethylphenidate mainly in the lower gastrointestinal tract, approved for ADHD from age 6. The duration comes from delayed prodrug conversion rather than from a bead or osmotic delivery system, so nothing in the capsule can be damaged by chewing or sprinkling. Its milligram numbers do not compare with any other methylphenidate product. Schedule II; brand only.

Forms & Strengths

- Capsules (serdexmethylphenidate / dexmethylphenidate): 26.1 mg / 5.2 mg, 39.2 mg / 7.8 mg, 52.3 mg / 10.4 mg

Dosing

- **Age:**
  - 6-12 y/o: established by a controlled trial and a 12-month open-label safety study
  - 13-17 y/o and adults: established by pharmacokinetic bridging
  - Under 6 y/o: not recommended; higher plasma exposure and more adverse reactions, including weight loss
- **Onset:** ~ 2 hours fasted, later with food
- **Duration:** up to 13 hours

- **Release Profile:** fixed molar ratio, 30% dexmethylphenidate to 70% serdexmethylphenidate. This is capsule composition, not a bead-release split: the long tail comes from prodrug conversion in the lower gut
- **Initial Dose:** 39.2 mg / 7.8 mg once daily in the morning, in every age band
- **Titration:**
  - 6-12 y/o: after 7 days, increase to 52.3 mg / 10.4 mg or decrease to 26.1 mg / 5.2 mg
  - 13-17 y/o and adults: after 7 days, increase to 52.3 mg / 10.4 mg; no labelled down-titration step
- **Max Dose:** 52.3 mg / 10.4 mg once daily, in every age band
- **Considerations:** Once daily in the morning; food delays the peak about 2 hours without changing exposure. Never substitute for another methylphenidate milligram for milligram; stop it and titrate from the standard start.

Pharmacology

- **Mechanism:** Blocks presynaptic dopamine and norepinephrine reuptake at DAT and NET; does not meaningfully promote catecholamine release at therapeutic doses. Serdexmethylphenidate is inactive until converted.
- **Delivery / Release:** Fixed molar ratio, 30% dexmethylphenidate to 70% serdexmethylphenidate. The free drug peaks at ~2 hours fasted; the prodrug converts in the lower gut and alone peaks at about 8 hours.
- **Metabolism:** The converting enzymes are unidentified; prodrug bioavailability is under 3%, and neither component is a CYP or transporter substrate. Half-life ~5.7 h (prodrug) and ~11.7 h (dexmethylphenidate, absorption-limited). Steady state by the third dose.
- **Class Positioning:** Duration comes from a prodrug rather than beads (Focalin XR) or an osmotic pump (Concerta), so there is no release mechanism to destroy by opening or chewing.

Indications

- **ADHD** (ICD-10: F90.0, F90.1, F90.2, F90.8, F90.9): patients 6 y/o and older, including adults

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Off-Label Uses

- **Narcolepsy** (ICD-10: G47.419): racemic methylphenidate carries the indication; this product does not. Insufficient.

- **ADHD in a child aged 4 to 5** (ICD-10: F90.x): behavioral parent training first (AAP 2019). Use below 6 is not recommended, and the lowest strength already equals 20 mg. Not the preschool option.
- **Where the evidence does not support use.** AHRQ 2024 grades stimulant head-to-head comparisons as low strength of evidence, so nothing supports the prodrug design outperforming a conventional long-acting methylphenidate, or any use outside ADHD in youth.

Contraindications & Warnings

- **Boxed Warning:** Abuse, misuse, and addiction, which can lead to substance use disorder, overdose and death. Assess risk before prescribing and monitor throughout.
- **Contraindicated:**
  - Hypersensitivity to serdexmethylphenidate, methylphenidate or any component; bronchospasm, rash and pruritus reported.
  - Concomitant MAOI, or within 14 days of stopping one; hypertensive crisis.
- **Use with caution:**
  - Structural cardiac abnormality, cardiomyopathy, serious arrhythmia or coronary disease; the label says avoid.
  - Pre-existing hypertension, because blood pressure and heart rate rise on stimulants.
  - Pre-existing psychosis or bipolar disorder; motor or verbal tics and Tourette's syndrome.
  - Open-angle glaucoma, raised intraocular pressure, or significant hyperopia.
  - Peripheral vasculopathy including Raynaud's; substance use disorder in patient or household.
- **Screen before starting:**
  - Cardiac disease by history, family history of sudden death, and exam. No routine ECG.
  - Personal and family history of tics or Tourette's syndrome.
  - Risk factors for mania; abuse and diversion risk; baseline height, weight, blood pressure and heart rate.

Drug Interactions

- **Other methylphenidate products:** not an interaction but a substitution hazard the label calls out. Never switch milligram for milligram in either direction; discontinue the other product and titrate from the standard starting dose.
- **MAOIs** (phenelzine, tranylcypromine, selegiline, linezolid, methylene blue): hypertensive crisis. Do not co-prescribe; allow 14 days after stopping.
- **Antihypertensives** (any class): effectiveness may fall. Monitor blood pressure and adjust their dose.

- **Halogenated anesthetics** (sevoflurane, isoflurane, desflurane): sudden intraoperative pressure and rate rise. Avoid on the day of surgery.
- **Risperidone:** a dose change either way may raise EPS risk. Monitor for EPS across any change.

Administration

- Once daily in the morning, with or without food. A meal does not change exposure but pushes the peak to 4 or 4.5 hours.
- Swallow whole, or empty the contents into 50 mL of water or 2 tablespoons of applesauce and consume it all within 10 minutes of mixing.
- There is no release mechanism to destroy; the delay is in the prodrug chemistry.
- **Switching from another methylphenidate:** stop that product and start at 39.2 mg / 7.8 mg. Never convert by milligrams.
- Stop the drug if a month of dose adjustment brings no improvement. Store securely, preferably locked.

Side Effects

- **Common** (pooled methylphenidate class rates; no product-specific table exists): decreased appetite, decreased weight, nausea, abdominal pain, vomiting, insomnia, anxiety, affect lability, irritability, increased blood pressure, tachycardia.
- **Serious:**
  - Sudden death with structural cardiac disease; avoid use, and evaluate exertional syncope promptly.
  - New psychosis or mania, including with no psychiatric history; consider discontinuing.
  - Priapism, sometimes requiring surgery, including during drug holidays. Immediate care.
  - Peripheral vasculopathy including Raynaud's; reduce dose or stop.
  - Growth suppression: over 12 months in children 6-12, mean z-score change was minus 0.20 for weight and minus 0.21 for height, most in the first 4 months.
  - Acute angle closure glaucoma and raised intraocular pressure.
  - Hypersensitivity: bronchospasm, rash and pruritus reported with this product.

Monitoring & Labs

- **Substitution errors:** at every refill and transition of care, confirm no milligram conversion to or from another methylphenidate. The label warns this risks overdose.

- **Growth:** height, weight and BMI at baseline, monthly for the first 4 months, then every 6 months. Most weight z-score loss occurs in those 4 months.
- **Cardiovascular:** blood pressure and heart rate at baseline, at every dose change, and at least every 6 months; a sustained or symptomatic rise triggers dose reduction.
- **Appetite and sleep:** at every visit and dose change. Coverage runs to about 13 hours, so confirm the dosing time before treating insomnia as a dose problem.
- **Psychiatric, tics and digits:** screen for new psychosis, mania, aggression and emergent tics at every visit; inspect fingers and toes.
- **Abuse and diversion:** at every refill reassess risk, reconcile the pill count, and check the state PDMP per state requirement.

Discontinuation & Taper

- May be stopped abruptly at therapeutic doses; this label gives no taper instruction.
- After prolonged use expect withdrawal: dysphoria, fatigue, vivid dreams, sleep change, increased appetite, agitation.
- Priapism has occurred during withdrawal and planned holidays; mention it before a holiday in an adolescent male.
- Drug holidays are reasonable where appetite or growth limits treatment; the growth data make that a first-year conversation. No partial dose exists below 26.1 mg / 5.2 mg.

Pregnancy & Lactation

- **Pregnancy:** No data on Azstarys itself; methylphenidate studies have not identified a drug-associated risk. Stimulants reduce placental perfusion. Delayed fetal ossification in rats at 3 times the maximum human dose.
- **Lactation:** No data on serdexmethylphenidate in milk. For the dexmethylphenidate component, infant doses were 0.16% to 0.7% of the maternal dose. Monitor for agitation, poor feeding and low weight gain.
- **Dexmethylphenidate specifically:** a maternal requirement is not a reason to stop breastfeeding; large doses may interfere before lactation is established. (LactMed 2025)
- **Exposure Registry:** National Pregnancy Registry for Psychostimulants, 1-866-961-2388

Counseling Points

- **Counsel the family on:**
  - Why the milligram numbers look large: most of the capsule is prodrug, inactive until the gut converts it. The 39.2/7.8 mg capsule equals about 30 mg of dexmethylphenidate.

    - That no other ADHD medication converts to this one by milligrams, so any substitution must be checked with the prescriber first.
    - Coverage running to roughly 13 hours, so a late-morning dose still works at bedtime. Keep the dose time fixed and early.
    - That opening the capsule into water or applesauce is a labelled option, but the mixture must be finished within 10 minutes.
    - Appetite suppression, largest in the first 4 months: move the largest meal to breakfast and to the evening.
    - Locked storage, and that sharing a Schedule II medication is a felony.
- **Advise them to call for:**
    - Chest pain, fainting, or a racing heart that does not settle.
    - New hallucinations, or new suspicious, fearful or grandiose thinking.
    - Wheeze, rash or itching after a dose, reported with this product specifically.
    - Numbness or colour change in the fingers or toes; eye pain or blurred vision.
    - A new tic, or a marked worsening of an existing one.
    - Weight loss, or clothes fitting more loosely, particularly in the first 4 months.
    - A painful erection lasting more than a few hours, including during a planned break.

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