STIMULANT C-II

Dexmethylphenidate

Focalin, Focalin XR, Azstarys (with serdexmethylphenidate)

The active d-enantiomer of methylphenidate, given at half the racemic dose for the same effect with less inert isomer load.

USUAL ADULT RANGE	HALF-LIFE	METABOLISM	ONSET
IR 10-20 mg/d; XR 10-40 mg/d	2-4.5 h; XR covers ~12 h	CES1A1 to d-ritalinic acid	30 min; IR lasts 4-6 h

⚠ FDA BOXED WARNING

Abuse, misuse, addiction, and dependence: dexmethylphenidate 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 cause overdose and death. Assess risk before prescribing and monitor throughout treatment.

INDICATIONS

- FDA-approved for attention-deficit/hyperactivity disorder in patients age 6 years and older as immediate-release tablets and as Focalin XR capsules.
- Azstarys, a fixed combination of the prodrug serdexmethylphenidate with dexmethylphenidate, is approved for ADHD in patients age 6 and older.
- Preferred when a patient responded to racemic methylphenidate but disliked the tablet burden, since equal effect comes at half the milligram dose.
- Focalin XR is a useful once-daily option when the immediate-release form works but wears off before the end of the school or work day.
- Used off-label for narcolepsy and idiopathic hypersomnia, an indication carried by racemic methylphenidate but not by dexmethylphenidate products.
- Used off-label for apathy, fatigue, and cognitive slowing after traumatic brain injury and in medically ill or geriatric depressed adults.

DOSING & TITRATION

- Immediate-release: start **2.5 mg** PO twice daily at least 4 hours apart, raise weekly by **2.5-5 mg/day**, maximum **20 mg/day** in divided doses.
- When switching from racemic methylphenidate, start at half the total daily methylphenidate dose and retitrate from there.
- Focalin XR: adults start **10 mg** each morning to a maximum of **40 mg/day**; children 6-17 start **5 mg/day** to a maximum of 30 mg/day.
- Azstarys in patients 6-12 starts at 39.2/7.8 mg each morning; adolescents and adults start at the same dose, with a maximum of 52.3/10.4 mg daily.
- Capsules may be opened and sprinkled on applesauce and taken immediately; beads must not be crushed or chewed, which would dump the whole dose.
- No labeled renal or hepatic adjustment; stop for emergent psychosis, unmanageable insomnia, or a sustained rise in blood pressure rather than dose-reduce forever.

MECHANISM OF ACTION

- Blocks the dopamine and norepinephrine transporters, increasing synaptic catecholamines in prefrontal cortex and striatum without forcing vesicular release.
- Contains only the d-threo enantiomer, the isomer that carries essentially all transporter affinity in the racemic mixture.
- Because the largely inert l-threo isomer is absent, milligram-for-milligram potency is roughly twice that of racemic methylphenidate.
- Enhanced prefrontal norepinephrine and dopamine tone improves sustained attention, working memory, and response inhibition at moderate doses.
- In Azstarys, serdexmethylphenidate is converted to dexmethylphenidate in the lower gastrointestinal tract, giving delayed second-phase coverage.

PHARMACOKINETICS

- Immediate-release Tmax is 1-1.5 hours; Focalin XR is bimodal with peaks near 1.5 hours and 6.5 hours from its two bead populations.
- Half-life is about 2.2 hours in children and 3 hours in adults, while clinical coverage is 4-6 hours for IR and roughly 12 hours for XR.
- Metabolized by carboxylesterase CES1A1 to inactive d-ritalinic acid; CYP450 involvement is negligible, so most CYP-based interactions do not apply.
- A high-fat meal delays Focalin XR Tmax by about 1 hour but does not change overall exposure, so it can be taken with or without food.
- About 90 percent of the dose appears in urine as d-ritalinic acid, and protein binding is low, near 12-15 percent.

ADVERSE EFFECTS

- Decreased appetite in about 30 percent, insomnia in 15-20 percent, headache, abdominal pain, dry mouth, irritability, and jitteriness are common.
- Rebound irritability and hyperactivity as the dose wears off is more noticeable with immediate-release dosing than with the XR form.
- Modest rises in blood pressure and heart rate of roughly 2-4 mmHg and 3-6 bpm, with occasional clinically meaningful hypertension or tachycardia.
- Weight loss and slowed growth velocity in children, so weight and height should be tracked and drug holidays considered if growth deviates.
- New psychosis, mania, or worsening tics can appear at usual doses and warrant stopping the stimulant rather than adding another medication.
- Priapism and peripheral vasculopathy including Raynaud phenomenon are labeled warnings; digital numbness or ulceration requires reassessment.

MONITORING

- Baseline weight, height, pulse, blood pressure, cardiac and family sudden-death history, and screening for tics, psychosis, and substance misuse.
- Repeat vital signs and weight each visit, with height plotted at least every 6 months in children and adolescents on continuous treatment.
- Use ADHD-RS-5, Vanderbilt, or Conners ratings before and after each dose change to separate real benefit from expectancy.
- Ask specifically about end-of-dose rebound, evening appetite return, and sleep onset time, since these drive formulation and timing choices.
- Check the prescription drug monitoring program and reassess misuse or diversion risk at every refill of this schedule II product.

INTERACTIONS & CAUTIONS

- Contraindicated within 14 days of an MAOI, including phenelzine, tranylcypromine, selegiline, and linezolid, because of hypertensive crisis risk.
- May inhibit metabolism of warfarin, phenytoin, phenobarbital, and tricyclic antidepressants, so check levels or INR when these are combined.
- Additive sympathomimetic effects with decongestants, other stimulants, and SNRIs raise blood pressure and heart rate; recheck vitals after adding either.
- Halogenated anesthetics can cause sudden blood pressure and heart rate swings, so hold the dose on the day of an elective procedure.
- Alcohol accelerates release from some extended-release formulations, producing dose dumping and an unintended immediate-release exposure.

SPECIAL POPULATIONS

- Pregnancy: limited data with no clear teratogenic pattern; use only if benefit clearly outweighs risk and prefer nonpharmacologic strategies first.
- Lactation: methylphenidate enantiomers pass into milk in very low amounts, and most infants tolerate maternal treatment without observed effects.
- Pediatric: labeled from age 6; use in children under 6 is off-label and behavioral parent training should be first-line at that age.
- Geriatric: no dedicated studies, so start at the lowest dose and monitor blood pressure, arrhythmia, appetite, and sleep closely.
- Renal and hepatic impairment: no dose adjustment is labeled since clearance depends on carboxylesterase rather than hepatic CYP or renal excretion of drug.

PRESCRIBING PEARLS

- Dexmethylphenidate 10 mg roughly equals racemic methylphenidate 20 mg; halve the dose when switching.
- Focalin XR peaks twice, so an early afternoon slump often means timing, not dose, is the problem.
- Azstarys reaches full effect faster than most prodrug stimulants because part of the dose is already active.

Verify against the current FDA label and your formulary before prescribing. Educational reference only.

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.