NON-STIMULANT ADHD AGENT

Atomoxetine

Strattera

Selective norepinephrine reuptake inhibitor for ADHD; no abuse liability, but effect is smaller and slower than with stimulants.

USUAL ADULT RANGE	HALF-LIFE	METABOLISM	ONSET
40-100 mg/day PO	5 h; 22 h if CYP2D6 PM	CYP2D6 substrate; CYP2C19	1-2 wks; 4-6 wks full effect

⚠ FDA BOXED WARNING

Suicidal ideation in children and adolescents: atomoxetine increased suicidal ideation in short-term pediatric trials (0.4 percent versus none with placebo, no completed suicides). Monitor closely for suicidality, clinical worsening, and unusual behavior change, especially early in treatment and after dose changes.

INDICATIONS

- FDA-approved for attention-deficit/hyperactivity disorder in children age 6 years and older, adolescents, and adults as monotherapy.
- First-line non-stimulant when there is active substance misuse, diversion risk, or a patient or family preference against controlled substances.
- Preferred when stimulants worsen comorbid anxiety, tics, or insomnia, since atomoxetine does not aggravate these and covers 24 hours.
- Used off-label as an add-on to a stimulant for residual evening or early morning symptoms, though combination data remain limited.
- Used off-label for ADHD symptoms in adults with comorbid anxiety disorders, where trials show benefit for both symptom domains.
- Not effective for narcolepsy, binge eating disorder, or as an antidepressant, despite its noradrenergic mechanism.

DOSING & TITRATION

- Children and adolescents up to 70 kg: start **0.5 mg/kg/day** PO, increase after at least 3 days to a target of about **1.2 mg/kg/day**.
- Maximum in patients up to 70 kg is **1.4 mg/kg/day** or **100 mg/day**, whichever is less, given once in the morning or split twice daily.
- Adults and patients over 70 kg: start **40 mg/day**, increase after at least 3 days to **80 mg/day**, with a maximum of **100 mg/day**.
- Known CYP2D6 poor metabolizers and patients on strong CYP2D6 inhibitors should start at 0.5 mg/kg/day and increase only after 4 weeks.
- Hepatic impairment: reduce to 50 percent of the usual dose in Child-Pugh class B and to 25 percent in Child-Pugh class C.
- No taper is needed on discontinuation, and no rebound hyperactivity or withdrawal syndrome occurs when it is stopped.

MECHANISM OF ACTION

- Selectively inhibits the presynaptic norepinephrine transporter, raising synaptic norepinephrine throughout cortical and subcortical circuits.
- In prefrontal cortex, where dopamine is largely cleared by the norepinephrine transporter, it also raises prefrontal dopamine.
- It does not increase dopamine in nucleus accumbens or striatum, which explains the absence of euphoria and abuse liability.
- Enhanced tonic prefrontal catecholamine signaling improves attention and impulse control gradually rather than dose by dose.
- Because the effect depends on receptor adaptation rather than acute release, benefit accrues over weeks and persists overnight.

PHARMACOKINETICS

- Rapidly absorbed with Tmax of 1-2 hours; food slows absorption modestly and reduces peak concentration, which can lessen nausea.
- Metabolized primarily by CYP2D6 to the equipotent 4-hydroxyatomoxetine, with CYP2C19 providing a minor pathway.
- Half-life is about 5 hours in extensive metabolizers but 22 hours in poor metabolizers, who have roughly tenfold higher exposure.
- Approximately 7 percent of White and 2 percent of Black patients are CYP2D6 poor metabolizers, a group with more adverse effects.
- Hepatic impairment increases exposure substantially, requiring a 50 percent dose reduction in Child-Pugh B and 75 percent in Child-Pugh C.

ADVERSE EFFECTS

- Nausea, decreased appetite, dry mouth, fatigue, insomnia, and dizziness are the common effects and often improve after the first few weeks.
- Adults report urinary hesitancy or retention, erectile dysfunction, and dysmenorrhea more often than children do.
- Small mean rises in heart rate of about 5-10 bpm and in blood pressure of 2-4 mmHg, with orthostatic hypotension and syncope reported.
- Severe hepatic injury is rare but real, presenting as jaundice, dark urine, or transaminase elevation and requiring permanent discontinuation.
- Priapism has been reported in children and adults, and any erection lasting over 4 hours needs urgent evaluation.
- Growth in children slows early, with weight and height typically returning toward baseline percentiles over 2-3 years of treatment.

MONITORING

- Baseline and periodic height, weight, blood pressure, and pulse, including orthostatic vitals in patients reporting dizziness.
- Ask about suicidal thoughts, agitation, irritability, and unusual behavior at every visit in the first months, especially in youth.
- Liver chemistry is not required routinely, but obtain transaminases and bilirubin promptly for jaundice, dark urine, or right upper quadrant pain.
- Use a validated rating scale at baseline and at 4 and 8 weeks, because a fair trial takes at least 6 weeks at target dose.
- Consider CYP2D6 genotyping when adverse effects appear at low dose or when there is no response at maximal dose.

INTERACTIONS & CAUTIONS

- Contraindicated within 14 days of an MAOI because of the risk of serious, sometimes fatal, hypertensive and hyperthermic reactions.
- Strong CYP2D6 inhibitors such as paroxetine, fluoxetine, bupropion, and quinidine raise exposure several-fold, so titrate slowly and cap the dose.
- Contraindicated in narrow-angle glaucoma, pheochromocytoma, and severe cardiovascular disease including serious structural cardiac abnormality.
- Pressor agents including albuterol and decongestants can produce additive increases in blood pressure and heart rate.
- Additive cardiovascular effects with stimulants and with drugs that prolong the QT interval warrant closer vital sign monitoring.

SPECIAL POPULATIONS

- Pregnancy: human data are limited and no clear teratogenic pattern is known; use only when the benefit justifies the potential fetal risk.
- Lactation: minimal published data on transfer into human milk, so monitor the breastfed infant for irritability and poor feeding.
- Pediatric: approved from age 6 years; the suicidality boxed warning applies specifically to children and adolescents.
- Geriatric: safety and effectiveness have not been established in patients over 65, and orthostatic effects are more consequential.
- Hepatic impairment requires substantial dose reduction, while renal impairment does not require dose adjustment.

PRESCRIBING PEARLS

- It is not a rescue drug; judge it at 6 weeks on target dose, not at week 1.
- Fluoxetine or paroxetine turns almost any patient into a CYP2D6 poor metabolizer; start low.
- Dosing at night with food often solves both the nausea and the sedation complaints.

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

Eli Lilly and Company. (2025). *Strattera (atomoxetine hydrochloride) capsules [Prescribing information]*. U.S. Food and Drug Administration. https://dailymed.nlm.nih.gov/dailymed/

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

National Institute of Diabetes and Digestive and Kidney Diseases. (2020). Atomoxetine. In *LiverTox: Clinical and research information on drug-induced liver injury*. https://www.ncbi.nlm.nih.gov/books/NBK548671/

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

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.