ADHD Medication Review – June 2025

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Benefits of ADHD medication outweigh health risks, study finds
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🧪 Solriamfetol (Sunosi) – Adult ADHD, in Phase 3

- **FOCUS trial (Phase 3, adults, 516 participants)**:
  - Demonstrated a **~50% reduction** in symptom burden (measured via AISRS) over 6 weeks, with statistically significant improvements vs placebo (17.7-point drop for 150 mg vs 14.3 for placebo; P=0.039) technologynetworks.com+2globenewswire.com+2psychiatrictimes.com+2psychiatrictimes.com+1fiercepharma.com+1.
  - **Achieved primary and key secondary endpoints**, including Clinical Global Impression of Severity (CGI-S) improvement (P=0.017) contemporarypediatrics.com+4psychiatrictimes.com+4biospace.com+4.
  - **Onset noted by week 1** for symptom improvement en.wikipedia.org+8psychiatrictimes.com+8biospace.com+8.
  - Safety profile: well tolerated; side effects dose-dependent; **no serious adverse events** globenewswire.com+15globenewswire.com+15psychiatrictimes.com+15.
- **Next steps**:
  - Paediatric Phase 3 now enrolling in 2025 globenewswire.com+9globenewswire.com+9biospace.com+9.
  - Exploring MDD with excessive daytime sleepiness (EDS); subgroup data supports a dedicated Phase 3 trial in 2025 appliedclinicaltrialsonline.com+3globenewswire.com+3sec.gov+3.
  - Registered trials ongoing for binge eating disorder and shift work disorder (topline anticipated in 2026) sec.gov.
- **Mechanism**:
  - Dual-action dopamine-norepinephrine reuptake inhibitor (DNRI), also TAAR1 agonist—sets it apart from classical stimulants en.wikipedia.org+1sec.gov+1.
  - Half-life ~7 hours; high oral bioavailability; low protein binding clinicaltrialvanguard.com+13en.wikipedia.org+13en.wikipedia.org+13.
  - Schedule IV controlled substance (lower misuse potential than amphetamines) en.wikipedia.org+1psychiatrictimes.com+1.

CTx-1301 – Once-Daily Extended-Release Dexmethylphenidate

- **Paediatric and adolescent Phase 3 trials (ages 6–17)**:
  - All fixed doses (18.75 mg, 25 mg, 37.5 mg) produced **significant symptom reduction** within 5 weeks. Effect sizes ranged from **0.74 to 1.19**, classified as large contemporarypediatrics.com+3drugtopics.com+3stocktitan.net+3.
  - Food-effect study showed flexibility—can be taken with or without food stocktitan.net+1clinicaltrialvanguard.com+1.
  - **No serious treatment-emergent adverse events** across trials clinicaltrialvanguard.com.
- **Adult data & FDA strategy**:
  - Combined adult/paediatric safety results presented at pre-NDA FDA meeting on April 2, 2025 contemporarypediatrics.com+2clinicaltrialvanguard.com+2globenewswire.com+2sec.gov+4globenewswire.com+4clinicaltrialvanguard.com+4.
  - NDA submission anticipated mid-2025 biospace.com+6globenewswire.com+6sec.gov+6.
  - If approved, CTx-1301 would be the **first true once-daily stimulant covering an entire active day** without booster doses en.wikipedia.org+9contemporarypediatrics.com+9clinicaltrialvanguard.com+9.
- **Pharmacology**:
  - Extended-release dexmethylphenidate with a slightly longer half-life than existing ER formulations cingulate.com+15en.wikipedia.org+15drugtopics.com+15.
  - Utilizes “Precision Timed Release™” multi-core tablet designed to maintain therapeutic levels all day stocktitan.net+1globenewswire.com+1.

Onyda XR – First FDA-approved liquid non-stimulant

- **Extended-release clonidine suspension**, approved in 2024 for children aged 6+.
- Designed primarily for **night-time dosing**, either as monotherapy or adjunct to stimulants.
- Offers flexible titration and may reduce morning dosing issues—especially appealing to those with swallowing or dosing challenges.

Safety & Long-Term Use

- **Cardiovascular effects**: meta-analyses show **small increases** in heart rate and blood pressure from both stimulant and non-stimulant ADHD meds; guanfacine may slightly reduce them. These changes generally fall within tolerable ranges with appropriate monitoring.
- **Duration of use**: Finnish registry suggests most paediatric users remain on meds for >3 years, some extending 6–9 years, yet **long-term safety data beyond 12 months remains limited**.
- **Quality-of-life debate**: Emerging adult studies indicate symptom control does not always translate into sustained life-quality improvements—emphasizing the value of psychological, behavioural, and lifestyle interventions.

🧩 Integrative Clinical Implications

Medication	Patient Group	Advantages	Safety Notes
Solriamfetol	Adults (and soon paediatrics)	Rapid onset, dual mechanism, lower misuse risk	Monitor for insomnia, BP, anxiety
CTx-1301	Children/teens & adults	Once-daily coverage, strong effect sizes, flexible dosing	Standard stimulant monitoring
Onyda XR	Children 6+	Liquid form, bedtime dosing option, adjunct use	Watch for clonidine side effects
Existing options (e.g., guanfacine, methylphenidate ER/XR)	All ages	Established efficacy, varied formulations	Monitor cardiovascular, growth, sleep

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🔬 Emerging Pipeline and Other Innovations

- A number of agents remain under investigation or discontinued (e.g., certain nicotinic agonists, histamine H_3 antagonists, ampakines) contemporarypediatrics.comstocktitan.netclinicaltrialvanguard.com+1contemporarypediatrics.com+1en.wikipedia.org.
- The trend: **refinement of delivery systems** (e.g., time-release, liquids), **targeted non-stimulants**, and **combination approaches** (e.g., DNRI plus other receptor activity) are gaining traction.

✅ Summary: What This Means for Practice

1. **Solriamfetol** shows strong evidence for adult ADHD and expands to paediatric use—potentially offering a novel non-traditional stimulant.
2. **CTx-1301** may become a first-in-class once-daily stimulant offering consistent 24-hour symptom control with high effect sizes.
3. **Onyda XR** improves dosing flexibility for children with non-stimulants.
4. **Adverse events** continue to be manageable but warrant routine vital signs and growth/sleep monitoring.
5. **Long-term effects** are still unclear; multidisciplinary care remains essential.

🔶 Stimulants

Methylphenidate (e.g. Ritalin, Concerta)

- **Formulations**: Short-acting tablets, ER capsules (Concerta), and OROS systems.
- **Onset**: 30 min to 1.5 hrs; duration varies by formulation additudemag.com+15sparkmentalhealth.com+15qbtech.com+15en.wikipedia.org.
- **Efficacy**: Strong effect size in children and adults; executive function enhancement including working memory, response inhibition .
- **Side Effects**: Reduced appetite, sleep issues; small increases in BP/HR .

Amphetamines

- **Lisdexamfetamine (e.g., Vyvanse/Elvanse)**
  - Prodrug of dexamphetamine; ~1 hr conversion half-life ensures steady release and may lower misuse risk verywellhealth.com+3en.wikipedia.org+3ajmc.com+3en.wikipedia.org.
  - Most effective in adults per meta-analysis .
  - Same cardiovascular and appetite effects as methylphenidate.
- **Mixed Amphetamine Salts (e.g. Adderall XR)**
  - Rapid symptom control, risk of increased HR/BP, anxiety, especially in those with coexisting anxiety disorders theguardian.com+6en.wikipedia.org+6news-medical.net+6en.wikipedia.org+1verywellhealth.com+1verywellhealth.com.

🔷 Non-Stimulants

Atomoxetine (Strattera)

- SNRI approved for all ages ≥6 yrs en.wikipedia.org+1en.wikipedia.org+1.
- Onset: 1–4 weeks, full benefits may take up to a year en.wikipedia.org+1news-medical.net+1.
- Efficacy: Comparable to methylphenidate; slower onset, less misuse risk additudemag.com+15news-medical.net+15en.wikipedia.org+15.
- Side Effects: GI upset, possible increased HR/BP, rare severe adverse events, black-box warning for suicidal thoughts .

Viloxazine (Qelbree)

- Extended-release pricing repurposed SNRI approved for ages 6+ and adults .
- Comparable efficacy to atomoxetine and methylphenidate, with lower misuse liability en.wikipedia.org+3en.wikipedia.org+3adhdevidence.org+3.
- Side Effects: Drowsiness, headache, appetite suppression, rare seizures .

Alpha-2 Adrenergic Agonists (Guanfacine & Clonidine)

- **Guanfacine XR (Intuniv/Paxneury)**
  - For ages ≥6; reduces hyperactivity and impulsivity journals.healio.com+2en.wikipedia.org+2en.wikipedia.org+2.
  - Side Effects: Somnolence, low BP, dizziness; guanfacine can reduce HR/BP slightly .
  - New EU generic (Paxneury) authorized Feb 2025 en.wikipedia.org.
- **Clonidine ER**
  - Similar profile, often adjunctive for sleep and hyperactivity; available in liquid formulations.

🧩 Combination & Off-label

Azstarys (Serdexmethylphenidate + Dexmethylphenidate)

- FDA-approved March 2021 for ages 6+ en.wikipedia.org+10en.wikipedia.org+10en.wikipedia.org+10en.wikipedia.org.
- Offers both immediate and extended symptom control.
- Side Effects: Common stimulant-related ones—appetite loss, insomnia, jitteriness, increased HR/BP additudemag.com+11en.wikipedia.org+11news-medical.net+11.

Bupropion (Wellbutrin)

- Off-label use with efficacy similar to methylphenidate in ADHD news-medical.net.
- Side Effects: Lower misuse risk, but seizure potential; mood effects and cost-effective as generic.

⚖️ Comparative Overview

Medication	Class	Onset	Efficacy	Pros	Cons
Methylphenidate ER	Stimulant	0.5–1.5 hr	High	Long-used, varied formulations	Appetite loss, BP/HR increase
Lisdexamfetamine	Prodrug AMP	~1 hr conversion	Very high (esp. adults)	Smooth delivery, reduced misuse	Similar stimulant side effects
Atomoxetine	SNRI	1–4 weeks	Moderate	No abuse potential	Slow onset, GI, risk of mood changes
Viloxazine (Qelbree)	SNRI	Days–weeks	Moderate	Lower misuse potential, sprinkle capsules	Drowsiness, headache
Guanfacine XR	α2-agonist	~1 week	Moderate	Useful adjunct, BP-lowering	Sedation, hypotension, slow titration
Azstarys	Combo Stimulant	Immediate + extended	High	Smooth day coverage	Standard stimulant side effects
Bupropion	NDRI (off-label)	Weeks	Moderate	Generic, low abuse risk	Seizure risk, less evidence for ADHD

❓ Cardiovascular & Safety Context

- *Stimulants & non-stimulants* generally cause **modest increases** in heart rate and blood pressure—with guanfacine being the exception by reducing them somewhat en.wikipedia.org+4en.wikipedia.org+4news-medical.net+4en.wikipedia.org+3en.wikipedia.org+3verywellhealth.com+3sparkmentalhealth.com+1additudemag.com+1.

🧠 Clinical Takeaways

- **First-line in children & adults**: Stimulants (methylphenidate, amphetamines), extended releases preferred for consistency.
- **Non-stimulants (atomoxetine, viloxazine)**: Ideal if stimulants pose risks or in cases of substance misuse, anxiety, or cardiovascular concerns.
- **Alpha-2 agonists**: Useful adjuncts, especially for hyperactivity and night symptoms.
- **Off-label options**: Bupropion and others may fill gaps when classic meds are unsuitable.
- **Personalization**: Therapy choice should factor age, comorbidities, side effect sensitivity, abuse risk, and patient preference.

ADHD GENERAL NEWS

🏥 1. Adult ADHD clinical guidelines finally arriving

- **APSARD (American Professional Society for ADHD and Related Disorders)** is expected to release the first formal U.S. clinical guidelines for diagnosing and treating adult ADHD **by late 2025** chadd.org+10qbtech.com+10now.tufts.edu+10.
- This framework will cover diagnosis, pharmacotherapy, and non-medication strategies—largely filling a vital gap in primary care and mental health management now.tufts.edu.

💉 2. Long-term safety now under review

- A Finnish registry study shows that children and teens often remain on ADHD medications for an average of **3+ years**, with the longest quartile exceeding **7+ years** additudemag.com+5sciencedaily.com+5chadd.org+5.
- However, **reliable clinical safety data** beyond 12 months is scarce, putting focus on the need for extended outcome studies .

❤️‍🩹 3. Cardiovascular effects remain mild but monitored

- A major University of Southampton meta-analysis confirms stimulant and non-stimulant ADHD drugs cause **only small increases** in heart rate and blood pressure—except for guanfacine, which tends to **lower** them slightly additudemag.com+2southampton.ac.uk+2theguardian.com+2.
- Despite modest cardiovascular impact, this evidence reinforces the need for **routine monitoring protocols** in both children and adults .

🌎 4. Changing prescribing landscapes

- In New South Wales, Australia, **GPs will soon be authorized to diagnose and manage ADHD**, making it easier for families to access care locally (child prescriptions from **early 2026**) theguardian.com+1dailytelegraph.com.au+1.
- These reforms aim to reduce long waits, especially in regional areas, but also raise concerns about possible **overdiagnosis** without specialist oversight theguardian.com+1dailytelegraph.com.au+1.

🔬 5. Emerging non-stimulant compounds

Drug	Mechanism	Status
Centanafadine (Otsuka)	Triple reuptake inhibitor (serotonin, norepinephrine, dopamine)	Phase II/III adult ADHD trials ongoing theguardian.com+15en.wikipedia.org+15en.wikipedia.org+15
OPC-64005 (Otsuka)	SNDRI	ADHD development dropped after Phase 2; now focused on MDD
Pirepemat (IRLAB)	Cortical enhancer (multi-receptor effects)	ADHD program discontinued; being studied for Parkinson's cognition
Brilaroxazine (RP5063)	Dopamine-serotonin system modulator	Initially schizophrenia, now exploring ADHD indications

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🧩 6. Towards personalized and digital-enriched care

- Alongside pharmacotherapy, **digital and lifestyle interventions**—like neurofeedback, exercise monitoring, and AI-driven screening tools—are gaining momentum in the ADHD treatment ecosystem .
- Hybrid diagnostic algorithms (e.g., EEG-based deep learning models achieving ~90% accuracy) may eventually refine clinical assessment and reduce misdiagnosis arxiv.org.
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✅ In summary: What else is emerging now

- U.S. **adult ADHD guidelines** are imminent, which is a major shift in standardized care.
- **Long-term safety data for kids** remains limited—usage beyond 12 months is common, but evidence is not.
- **Australia's GP prescribing reforms** could reshape access—but require careful clinical training.
- A wave of **non-stimulant compounds** aiming for improved tolerability is in the pipeline.
- **Digital therapeutics and AI tools** are complementing medication, supporting personalized treatment pathways.