Whitepaper ADHD medication for Adults

Overview for specialist physicians who wish to initiate ADHD medication for their patients

Medication should:

- Be considered as first choice, unless the person prefers a non-medicinal approach
- Always be part of a broader treatment approach that also addresses psychological, behavioural, educational and/or work-related needs

1. Before starting ADHD medication

Required before initiation:

- Medical history and physical examination
  - Presence of exertion-related fainting, shortness of breath, and other cardiovascular symptoms/diseases
  - Pulse and blood pressure
  - Weight
- Family history
  - Cardiovascular diseases
  - Sudden death without clear cause <50 years
- ECG or referral to cardiologist in case of cardiac concerns in patient or family history
- Assess risk of substance misuse and medication misuse

2. Choice of medication

Methylphenidate of (Lis)dexamphetamine

- Both are first choice in the Belgian guideline
- Guideline advises primarily long-acting preparations (12h)
- Lisdexamfetamine is the safest choice when there is a risk of medication misuse

Not effective/poorly tolerated?

- Switch to the other first choice option (Methylphenidate or (Lis)dexamphetamine)
- Stimulants not effective: Atomoxetine
- Atomoxetine also not effective: off-label alternatives (or reassess for a missed diagnosis)

Good to know: Guanfacine has not yet been formally approved in Belgium for adults with ADHD, only for children and adolescents. It may be a possible off-label alternative, but be aware that there is currently insufficient research demonstrating its effectiveness in adults. Clonidine and Modafinil have also been studied, but so far there is likewise insufficient evidence to recommend their use in adults.

3. Dose titration

Starting dose

MEDICATION	STARTING DOSE
Methylphenidate	± 20 to 30 mg divided over 1–3 administrations per day
Lisdexamphetamine	30 mg, only in the morning
Dexamphetamine sulphate	Week 1: 2 × 2,5 mg/day Week 2: 2 × 5 mg/day Week 3: 2 × 7,5 mg/day Week 4: 2 × 10 mg/day
Atomoxetine	40 mg/day for 7 days, then increase to 80 mg/day

20 mg dexamphetamine sulphate ≈ 50 mg lisdexamphetamine ≈ 40 mg methylphenidate

Evaluating dose

AFTER 1 MONTH	Evaluate effects	Consider using the ASRS scale for structured comparison
	Evaluate side effects	If necessary follow up weight loss
	Pulse and blood pressure measurements	
	Decide on dose increase	Yes: increase the dose and re-evaluate again after 1 month No: continue monitoring with blood pressure/pulse measurement once every 6 months and follow-up on weight if needed
AFTER 1-2 YEARS	Assess whether tapering/stopping of medication is possible	Consider tapering in consultation with the patient The safety and effectiveness of medication use beyond 2 years in adults remains insufficiently studied

4. Different kinds of ADHD medication

Stimulantia

Methylphenidate

- Mechanism of action: Increases dopamine and noradrenaline by blocking synaptic reuptake
- Treatment effect from the first dose, with maximum effect after several weeks
- Maximum dosage according to guideline: 60–70 mg/day

DIFFERENT BRANDS OF METHYLPHENIDATE (IN BELGIUM)			
BRAND	**AFGIFTE**	**TMAX**	**T1/2**
Concerta	Delayed 22% immediate 78% regulated	Biphasic 1st: 1-2 hr 2nd: 6-8 hr	3,5 hr
Equasym	Delayed 30% immediate 70% regulated	Biphasic 1ste: 1,5 hr 2de: 4,5 hr	2 hr
Medikinet	Immediate	1-2 hr	2 hr
	Delayed 50% immediate 50% regulated	Biphasic 1ste: 1-2 hr 2de: 4 hr	3,2 hr
Methylfenidaat Retard	Delayed 22% immediate 78% regulated	Biphasic 1ste: 1-2 hr 2de: 6-8 hr	3,5 hr
Rilatine	Immediate	1-2 hr	2 hr
	Delayed 50% immediate 50% regulated	Biphasic 1ste: 1-2 hr 2de: 4 hr	3,5 hr

(Lis)dexamphetamine

- Mechanism of action: Increases dopamine and noradrenaline by stimulating release and blocking synaptic reuptake
- Treatment effect from the first dose, with maximum effect after several weeks
- Daily intake not always necessary
    - Lisdexamfetamine: metabolised to dexamphetamine via an enzyme in the blood; this is a rate-limiting step, which limits maximum brain exposure

- Maximum dosage according to guideline:
  - Dexamphetamine sulphate: 30 mg/day, exceptionally 40 mg/day
  - Lisdexamfetamine: 70 mg/day

KORT- EN LANGWERKEND	
Short	▪ More flexibility in the duration of action ▪ More control and smaller steps possible when titrating the dose
Long	▪ Convenience of once-daily dosing; often improves treatment adherence ▪ Reduces the risk of misuse

Common potential side effects

- Insomnia, loss of appetite, weight loss
- Headache, dry mouth, gastrointestinal complaints (nausea, abdominal pain), restlessness, tremor, nervousness
- With methylphenidate, possible worsening of comorbid psychiatric symptoms (anxiety, depression, emotional blunting, autism)

Rare serious side effects

- Increased heart rate and blood pressure: risk of cardiac arrhythmias or sudden heart problems in patients with underlying heart disease
- Worsening of anxiety, OCD symptoms, tics/Tourette's syndrome, depressive symptoms
- Possible agitation or (rarely) psychotic or manic symptoms at high doses

Contra-indications

- Known severe structural cardiac abnormalities or arrhythmias, untreated hypertension, untreated hyperthyroidism, glaucoma, pheochromocytoma
- Concurrent use of MAO inhibitors
- Active psychosis, untreated bipolar disorder
- Pregnancy and breastfeeding

Non stimulantia

Atomoxetine

- Selective norepinephrine reuptake inhibitor
- Mechanism of action: Inhibits the presynaptic norepinephrine (NE) transporter, increasing NE levels + possible indirect increase in dopamine
- Full therapeutic effect may require 6–8 weeks of continuous use
- Daily intake is always necessary
- Has no significant abuse potential
- Maximum dosage: 100 mg/day

Common potential side effects

- Nausea
- Insomnia, decreased appetite
- Headache, agitation or anxiety (especially at the start), tremor, sweating
- Increased heart rate and/or blood pressure
- Rare: orthostatic hypotension
- Rare: sexual dysfunction

Good to know: Encourage the patient to maintain the prescribed dosage, as most side effects subside after the first few days or weeks. Advise taking it with sufficient food and drink.

Rare serious side effects

- Liver damage
- Increased suicidality
- Urinary retention (especially in older men)

Contraindications

- If a cardiologist advises against use because the noradrenergic effect on blood pressure and/or heart rate is medically contraindicated
- Untreated hyperthyroidism, glaucoma, pheochromocytoma
- Concurrent use of MAO inhibitors
- Caution in patients with liver function disorders
- Pregnancy and breastfeeding

Plus punt: Advantage: Atomoxetine may be preferred in cases of comorbid anxiety or tic disorders, as it can sometimes improve these conditions (or at least has a lower likelihood of worsening them compared to stimulants).

Off-label

Bupropion

- Type: Atypical antidepressant (off-label for ADHD)
- Chemical: norepinephrine–dopamine reuptake inhibitor (NDRI)
- Mechanism of action: Blocks the reuptake of dopamine and norepinephrine
  - Mechanism overlaps with ADHD stimulants, but is less potent and more diffuse
- Maximum dosage according to guideline: 450 mg/day

Common potential side effects

1. Insomnia, decreased appetite, weight loss
2. May increase blood pressure and/or heart rate
3. Dry mouth, headache, nausea, agitation/anxiety, tremor, sweating, constipation

Rare serious side effects

- Seizures, especially above 300 mg/day or in individuals with a history of epilepsy or eating disorders (lowers the seizure threshold)

Contra-indications

- Caution in individuals with a history of epilepsy, bulimia, or anorexia nervosa (due to increased seizure risk)
- Concurrent use of MAO inhibitors, or withdrawal from alcohol/benzodiazepines
- Exercise caution in untreated anxiety disorders or psychosis

Verder lezen

- https://www.adhd-traject.be/nl/pagina/behandeling-adhd
  Website for children and adolescents under 18 years, frequently used within child and adolescent psychiatry as a reference source

- Cortese, Samuele et al. “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* vol. 5,9 (2018): 727-738. doi:10.1016/S2215-0366(18)30269-4

- Zhang L, Li L, Andell P, et al. Attention-Deficit/Hyperactivity Disorder Medications and Long-Term Risk of Cardiovascular Diseases. *JAMA Psychiatry.* 2024;81(2):178–187. doi:10.1001/jamapsychiatry.2023.4294

Bronnen

- Hoge gezondheidsraad België: guideline for the pharmacological treatment of ADHD https://www.health.belgium.be/sites/default/files/uploads/fields/fpshealth_theme_file/20210308_hgr-9547_adhd_vweb_0.pdf

- Bcfi.be en geassocieerde bijsluiters van bovenvernoemde medicatie

- The Maudsley “Prescribing Guidelines in Psychiatry” boek, 13th edition

- Prescribers Guide Stahls Essential Psychopharmacology