



Ways of thinking...



# The thinking...



“There is useful guideline/information on how to start/change/medication”

<https://www.nzfchildren.org.nz/...> Type ADHD

#### 4.4 Medicines used for attention deficit hyperactivity disorder (ADHD) Psychostimulants

[https://www.nzfchildren.org.nz/nzfc\\_2328?searchterm=methylphenidate](https://www.nzfchildren.org.nz/nzfc_2328?searchterm=methylphenidate)

Psychostimulants (methylphenidate, dexamfetamine, and lisdexamfetamine (prodrug of dexamfetamine)) are used first-line for the pharmacological treatment of ADHD in children aged over 5 years and adolescents.

Response rates to psychostimulants are high. Overall efficacy and tolerability are generally comparable across the different psychostimulants, although methylphenidate may be better tolerated in children and is often preferred. Individual responses vary considerably, approximately 70% of children respond to the first psychostimulant tried, and up to 90% show benefit if switched to an alternative. Therefore, if there is no meaningful improvement after a one-month trial at the maximum tolerated dose of a psychostimulant, switching to another psychostimulant is recommended.

## 4.4 Medicines used for attention deficit hyperactivity disorder (ADHD) Psychostimulants

[https://www.nzchildren.org.nz/nzfc\\_2328?searchterm=adhd](https://www.nzchildren.org.nz/nzfc_2328?searchterm=adhd)

### Methylphenidate

Effective dose usually 0.3-1.5mg/kg/day

Preparation	% immediate release (IR)	Release profile	Approx. onset of action (minutes)	Approx. duration (hours)	Advantages	Disadvantages
Immediate-release (IR) (tablet) <i>Ritalin</i> <sup>®</sup> / <i>Rubifen</i> <sup>®</sup>	100%	Monophasic (single peak)	20-30	3-4	<ul style="list-style-type: none"> <li>Rapid onset.</li> <li>Flexible dosing.</li> <li>Useful for initial dose titration.</li> </ul>	<ul style="list-style-type: none"> <li>Requires multiple daily doses (e.g. two to three times daily).</li> <li>Social stigma of school/work re-dosing.</li> <li>Wearing-off effect may be problematic.</li> </ul>
<i>Rubifen SR</i> <sup>®</sup> (tablet)	0%	Monophasic (gradual plateau, smooth release)	60-120	~6-8	<ul style="list-style-type: none"> <li>Duration may be sufficient to cover school/workday in a single dose.</li> <li>May be preferred in younger children because of shorter duration of action compared to other controlled release preparations.</li> <li>Less fluctuations in plasma concentrations compared to IR and possibly <i>Ritalin LA</i><sup>®</sup>/<i>Rubifen LA</i><sup>®</sup>—reduced 'wearing off' (rebound) effect.</li> </ul>	<ul style="list-style-type: none"> <li>Slower onset compared to IR (may leave gap in morning coverage).</li> <li>Less flexible titration (only available as 20 mg tablet).</li> <li>Cannot be crushed/spit (must be swallowed whole).</li> <li>Food can change onset and duration of effect (faster absorption with high fat meal).</li> <li>Additional dosing, e.g. after school/work, may be required to extend duration.</li> </ul>
<i>Ritalin LA</i> <sup>®</sup> / <i>Rubifen LA</i> <sup>®</sup> (capsule)	50%	Biphasic (two peaks), designed to mimic twice daily IR dosing	20-60	~8	<ul style="list-style-type: none"> <li>Mimics twice daily IR dosing in a single administration.</li> <li>Faster onset than <i>Rubifen SR</i><sup>®</sup> (above).</li> <li>Duration may be sufficient to cover school/workday in a single dose.</li> <li>Sprinkle option for those who cannot swallow tablets/capsules.</li> </ul>	<ul style="list-style-type: none"> <li>Midday dip possible before second peak.</li> <li>Additional dosing, e.g. after school/work, may be required to extend duration.</li> </ul>
<i>Concerta</i> <sup>®</sup> / <i>Methylphenidate ER</i> (Teva) <sup>®</sup> / <i>Methylphenidate Sandoz XR</i> <sup>®</sup> (tablet)	22%	IR coat with steady sustained release; smooth plateau	20-60	10-12*	<ul style="list-style-type: none"> <li>Longest coverage (about 12 hours).</li> <li>Flatter, smoother profile.</li> <li>Faster onset than <i>Rubifen SR</i><sup>®</sup>.</li> </ul>	<ul style="list-style-type: none"> <li>Less flexible dose titration.</li> <li>Cannot be crushed/spit (must be swallowed whole).</li> <li>Some children prefer more pulsed effect.</li> </ul>

## 4.4 Medicines used for attention deficit hyperactivity disorder (ADHD) Psychostimulants

### Dexamfetamine and lisdexamfetamine

Dexamphetamines effective dose usually 0.15-0.75mg/kg. If started due to intolerance of methylphenidate; consider starting even lower, going slower.

Dexamfetamine has a short duration of action (3–6 hours) requiring multiple daily doses, and there is currently no modified-release preparation approved in New Zealand. However, lisdexamfetamine (a prodrug) is gradually converted to dexamfetamine in red blood cells, and has an extended duration of action of 13 to 14 hours. For more information on lisdexamfetamine see [Spotlight on lisdexamfetamine](#) Prescriber Update, March 2024.

Due to differences in metabolism, there is no advantage of using dexamfetamine to determine an optimal lisdexamfetamine dose, as dose-equivalence between these two preparations cannot be determined. It is also not possible to determine dose-equivalence between methylphenidate and dexamfetamine or lisdexamfetamine—each must be titrated independently, see individual drug monographs.

## 4.4 Medicines used for attention deficit hyperactivity disorder (ADHD)

### Psychostimulants

#### Adverse effects of psychostimulants

##### Weight loss and growth deceleration

Reduced appetite, weight loss, and growth deceleration are common (see Monitoring for psychostimulants, below). Management strategies include:

- administering doses during or after meals
- using high calorie nutrient-rich foods (e.g. nuts, avocado)
- having large breakfast (prior to psychostimulant dose) and/or additional evening snacks once psychostimulant has worn off.

If these approaches are not sufficient, drug holidays (see below), dose reduction, or changing to atomoxetine (or alternative medicine for ADHD) can be considered.

##### Sleep disturbances

Psychostimulants can affect sleep, but insomnia is also common in children with ADHD and may stem from difficulty “switching off” active thoughts. It is therefore important to distinguish whether sleep difficulties are caused by the psychostimulant itself or by a wearing-off effect of the psychostimulant. If insomnia is directly medicine-related, using a shorter-acting preparation or administering the dose earlier in the day may help. Conversely, if sleep difficulties arise from a return of ADHD symptoms (after the psychostimulant has worn off), a small evening dose of psychostimulant can improve sleep onset. Regardless of the cause, behavioural strategies and good sleep-hygiene practices should always be encouraged.

##### Adverse effects on mood and behaviour

If adverse effects on mood and behaviour (e.g. anxiety, agitation, aggression, irritability, restlessness, depression) are noticed, it is important to establish timing of behavioural difficulties in relation to the dose to determine whether it is due to excessive dosing, or a wearing-off effect. If it is the latter, changing to a longer-acting formulation or providing an additional dose before the behaviour recurs may help. Psychostimulants should be immediately discontinued and specialist advice sought if psychosis or mania develop.

##### Increased blood pressure and heart rate

If blood pressure is consistently elevated with a psychostimulant (and was not found to be elevated prior to psychostimulant initiation), and this does not respond to dose reduction, the recommendation would be to discontinue the medicine and then recheck blood pressure. Once blood pressure has normalised, then one can trial an alternative medicine in the first instance. There is more concern with this adverse effect with psychostimulants than with atomoxetine, and it seems more problematic with higher doses (above 45 mg/day methylphenidate) and more persistent use.

## 4.4 Medicines used for attention deficit hyperactivity disorder (ADHD)

### Psychostimulants

#### Cautions and contra-indications for psychostimulants

##### Psychiatric comorbidities

Psychiatric comorbidities are common, anxiety and depression often accompany ADHD. Psychostimulants should be used with caution as they can increase anxiety and agitation particularly during treatment initiation. However, some cases of anxiety and depression may be secondary to untreated ADHD, and therefore treating the core symptoms of ADHD with psychostimulants may help reduce symptoms of anxiety and depression longer-term.

Psychostimulants are contra-indicated in the presence of **acute** severe mental illness including severe depression, agitated states, suicidal ideation, psychosis, mania, and anorexia nervosa. Once these disorders are appropriately treated and controlled psychostimulants may be considered. Specialist advice must be sought if there is a history of severe mental illness, and close supervision must be implemented.

##### Substance misuse

ADHD is common among individuals who misuse substances. Although some manufacturers contra-indicate psychostimulants when there is a risk of misuse, in some cases, appropriate treatment of ADHD may help reduce substance misuse. Non-stimulants may be preferred in this context; however, psychostimulant medicines can be considered on a case-by-case basis with specialist input. If psychostimulants are used, either modified-release methylphenidate or lisdexamfetamine are preferred due to their lower potential for misuse compared to immediate-release methylphenidate or dexamfetamine.

##### Tic disorders

ADHD is commonly seen in children with tic disorders. Although the manufacturer contra-indicates use of lisdexamfetamine in children with tics and cautions use of methylphenidate and dexamfetamine, psychostimulants do not always worsen tics. In some cases, tics may improve when ADHD is effectively treated, as reduced anxiety (secondary to ADHD) can decrease tic severity. Psychostimulants may therefore be considered under specialist guidance with close monitoring, particularly when tics are mild and the potential benefits outweigh the risks. Non-stimulants are preferred when tics are more severe or if they worsen with psychostimulant treatment.

##### Cardiovascular disease

Specialist advice must be sought for children with underlying cardiovascular disease before commencing treatment with psychostimulants (see Monitoring for psychostimulants below). Psychostimulants may increase heart rate and blood pressure, and caution is advised if the underlying cardiovascular disease is compromised by increases in blood pressure or heart rates. Psychostimulants have been associated with sudden cardiac death, therefore they are contra-indicated in children with severe cardiovascular disease, structural cardiac abnormalities, or cerebrovascular disorders.

For further cautions and contra-indications see also individual monographs.