



Stimulant Dosing Strategies to Cover the Day for Your Patient with ADHD

Objectives

- Describe stimulant dosing equivalences between immediate-release (IR) and extended-release (XR, or ER) formulations
- Assess the ADHD symptom coverage needs of individual patients
- Create dosing regimens that best meet your patients' needs

Case: Michael is an 8-year-old with ADHD combined type who has been taking dexamethylphenidate (DexMPH) XR 10 mg for 3 months. He has much improved focus and behavior at school. However, he goes to an afterschool program where he is impulsive, disruptive and does not get any of his homework done despite being given time to do it.



What should you do?

1. add a supplemental dose of dexMPH 10 mg at 3 pm
2. add a supplemental dose of dexMPH 5 mg at 3 pm
3. switch to amphetamine/dextroamphetamine 20 mg q am
4. encourage a predictable schedule, including regular bedtime, mealtimes, exercise and consistent rules and expectations

We will discuss the answer at the end of this guide.

Covering the day

You can almost always find a stimulant formulation or combination of formulations to your patients ADHD symptom control across their days.

To do this you need to understand 2 things:

- The duration of action of the formulations
- The dosage-release pattern of extended-release formulations

Here is a quick review of pharmacotherapy for ADHD. Stimulants are considered first-line treatment because of their effectiveness, versatility, and tolerability. Non-stimulants are also effective and provide continuous coverage when taken daily as prescribed. Non-stimulants are used alone or as augmentation to stimulant medications.

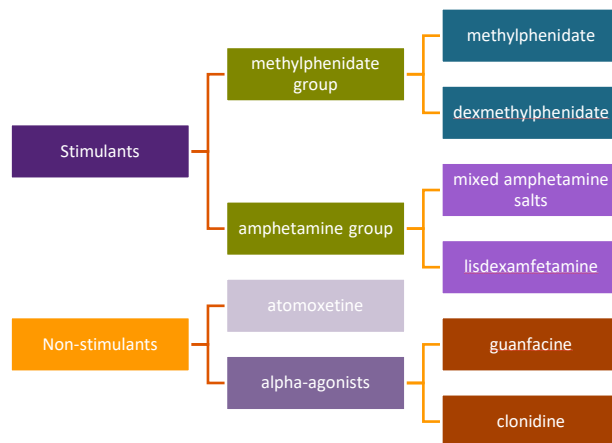
Stimulants

- Most effective
- Rapid onset; time-limited effect
- Can titrate periods of need
- Controlled substances (Schedule II)

Non-stimulants

- Also effective
- Provide continuous coverage
- Must be taken daily to work
- Not controlled substances

Stimulants fall into 2 groups: the methylphenidate group and the amphetamine group. Non-stimulants include 2 separate classes of medication: atomoxetine, and the alpha-agonists. We discuss stimulants only here.



We will start with stimulants in the methylphenidate group. This chart shows the duration of action of commonly used methylphenidate (MPH) and dexmethylphenidate (dexMPH) preparations. It also includes unit doses, which is the number of equivalent doses of immediate-release medication in each formulation.

Methylphenidate- and dexmethylphenidate- based stimulants

Medication	Expected duration of action	Number of unit doses	Administration options
methylphenidate IR (immediate release)	4 hours	1	crush
methylphenidate LA	6-8 hours	2	sprinkle
methylphenidate CD	6-8 hours	2	sprinkle
methylphenidate ER	10-12 hours	3	must swallow whole
dexmethylphenidate (immediate release)	4 hours	1	crush
dexmethylphenidate XR	8 hours	2	sprinkle

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The immediate release (IR) forms of MPH and dexMPH are also called short acting forms. These forms last about 4 hours each and are generally dosed morning, noon, and 3-4 pm if needed. The tablet sizes are listed here:

- methylphenidate: 5, 10, 20 mg tablets
- dexmethylphenidate: 2.5, 5, 10 mg tablets

Tablet forms may be crushed and mixed with soft food.

The first extended-release formulations of stimulants came to market in about 2000. The formulations developed from 1999 to 2006 all used some type of physical or mechanical strategy to push out discrete doses of medication similar to the way that you would administer repeated doses of immediate-release medication through the day.

MPH-CD or *Metadate CD* uses a pulsed strategy to deliver the equivalent of 2 doses of immediate-release MPH about 4 hours apart.

MPH-ER or *Concerta* uses an osmotic pump to deliver 3 doses of MPH, each about 4 hours apart. The conversion from short-acting methylphenidate to MPH-ER is shown here. This tablet is ineffective if cut or crushed.

Methylphenidate ER Doses

5 mg MPH tid → 18 mg MPH ER qd

7.5 mg MPH tid → 27 mg MPH ER qd

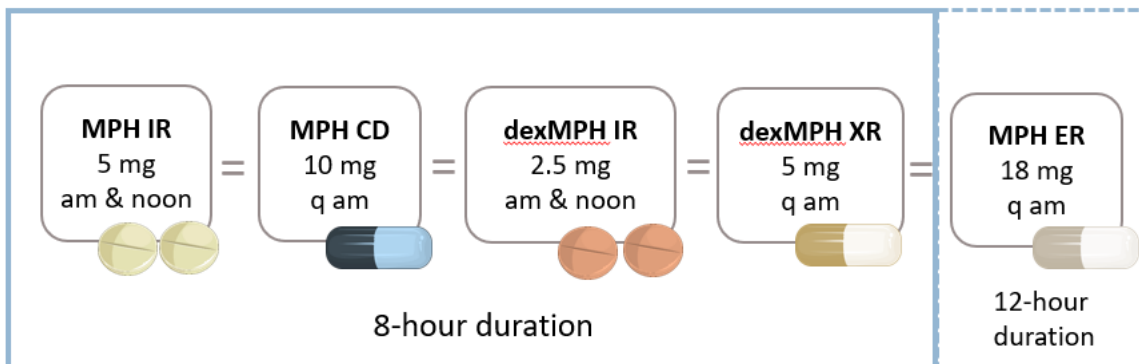
10 mg MPH tid → 36 mg MPH ER qd

15 mg MPH tid → 54 mg MPH ER qd

Some patients may require and tolerate 72 mg (FDA approved max)

Dexmethylphenidate is the D-isomer of methylphenidate and is sold as a generic and as brand name *Focalin*. It comes in an IR form that lasts about 4 hours, similar to methylphenidate, and an extended-release form that delivers 2 pulsed doses and lasts about 8 hours. Children who need ADHD symptom control after school hours may benefit from a supplemental dexmethylphenidate IR dose after school. This dose should be half of the XR dose. Because dexmethylphenidate is the d-isomer, dosing is half the methylphenidate dose.

This graphic shows equivalencies of the common formulations of MPH and dexMPH. If you want to cover an 8-hour day, your starting dose options are as shown. If you want to cover a 12-hour day at the same unit dose level, MPH ER 18 mg is one option. Note that the graphics do not represent exactly what the actual pills look like.



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Now we will look at the amphetamine-based stimulants. There are more formulations in this group, but we are focusing on the older, more common ones that tend to be on state formularies.

Medication	Expected duration of action	Number of unit doses	Administration options
mixed salts amphetamine IR (immediate release)	4-5 hours	1	crush
mixed salts amphetamine XR (extended release)	10 hours	2	sprinkle
lisdexamfetamine dimesylate	12 hours	monophasic	sprinkle or mix with liquid

The unit dose of immediate-release mixed-salts amphetamine, or *Adderall*, lasts a little longer than does a dose of immediate-release methylphenidate.

The extended-release form (*Adderall XR*) mimics *delivering 2 doses about 4-5 hours* apart and can come close in duration of action to methylphenidate given as 3 doses. Some patients will still need a supplemental after school dose.

Lisdexamfetamine dimesylate (LDX)

Rather than using a mechanical or physical mechanism to achieve a prolonged duration of action, LDX (*Vyvanse*) is a prodrug in which *d*-AMP is covalently bound to the amino acid lysine. LDX itself is therapeutically inactive but, after oral administration is hydrolyzed in the GI tract. It is dosed once daily and effective from 1.5 hours after dose until 12-13 hours after dose.

LDX has lower abuse potential than do other stimulants but is a still Schedule II drug.

Dosing starts at 20-30 mg. You can titrate up by 10 mg increments to a maximum recommended dose of 70 mg. The capsule may be opened and sprinkled on food or dissolved in water (stir thoroughly and take immediately).

So far, we have covered the older and more commonly used stimulant medications. The goal has been to help you think about how much medication any formulation delivers over how much time so that you can best meet your patient's need for ADHD symptom control. The charts below include a broader range of methylphenidate formulations, and of amphetamine formulations.

Methylphenidate group			
Generic/Brand Name(s)	Typical starting dose	FDA Max Dose/Day	Expected duration (hours)
immediate release methylphenidate and dexamethylphenidate formulations			
methylphenidate hcl tablet, chew-tab, oral solution			
Methylin®, Ritalin®	5 mg am & noon	60 mg	4
dexamethylphenidate tablet Focalin®	2.5 mg am & noon	20 mg	4
methylphenidate hcl and dexamethylphenidate extended release formulations			
Metadate ER® tablet	10 mg	60 mg	8
Metadate CD® capsule	20 mg	60 mg	8
Methylin ER® tablet	10 mg	60 mg	8
Ritalin LA® tablet	20 mg	60 mg	8
Ritalin SR® tablet	10 mg	60 mg	8
Concerta® OROS tablet	18 mg	72 mg	10 to 12
Apensio XR® capsule	10 mg	60 mg	12
Daytrana® patch	10 mg	30 mg	10 to 12
Quillivant XR® suspension	20 mg	60 mg	10 to 12
QuilliChew ER® chewable	20 mg	60 mg	10 to 12
<i>dexamethylphenidate extended release</i>			
Focalin® XR capsule	5 mg	30 mg	8

Amphetamine-related group			
Generic/Brand Name(s)	Typical starting dose	FDA Max Dose/Day	Expected duration (hours)
Immediate release amphetamine formulations			
Adderall® (amphetamine mixed salts tablet)	5 mg am & noon	40 mg	4 to 5
Procentra Oral Solution® (d-amphetamine solution)	5 mg am & noon	40 mg	4 to 5
Evekeo® (d- and l-amphetamine tablet)	5 mg am & noon	40 mg	4 to 5
Zenzedi (d-amphetamine tablet)	5 mg am & noon	40 mg	4 to 5
Extended release amphetamine formulations			
Adderall XR® (amphetamine extended release mixed salts capsule)	5-10 mg	30 mg	8 to 10
Dexadrine Spansule® (d-amphetamine sulfate extended-release capsule)	10 mg	40 mg	8
Vyvanse® (lisdexamphetamine capsule)	20 mg	70 mg	10 to 12
Dyanavel XR® (amphetamine extended release oral suspension)	2.5-5 mg	20 mg	13
Adzenys XR-ODT® (amphetamine ext-release orally disintegrating tablet)	6.3 mg	18.8 mg	10

Stimulant dose and duration of action

- If a stimulant is at an effective dose, its duration of action should be the expected duration of action.
- If a stimulant dose does not provide the expected duration of action, increasing the dose may get you to the expected duration of action.
- Once at the expected duration of action, increasing the dose will not make it last any longer.

What about Michael? Which is the best strategy? Remember, Michael was doing really well through an 8-hour school day with dexMPH XR 10 mg taken around 7 am. Let's go through the options.

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1. add a supplemental dose of dexMPH 10 mg at 3 pm: *DexMPH XR 10 mg is the equivalent of dexMPH IR 5 mg given in 2 doses, 4 hours apart. So adding a supplemental afternoon dose of dexMPH IR 10 mg, which is option A, would be doubling the unit dose and be way too much.*
2. **add a supplemental dose of dexMPH 5 mg at 3 pm:** *adding a supplemental dose of dexMPH 5 mg in the afternoon, is extending the same dosing pattern in the morning XR dose, and is **the correct answer**.*
3. switch to amphetamine/dextroamphetamine 20 mg XR q am: *switching to MAS or amph/dextroamph 20 mg XR (Adderall XR) might get you appropriate coverage for a longer period of time, up to 10-12 hours, but Michael is doing fine on the dexMPH, so there is no reason to switch right now.*
4. encourage a predictable schedule, including regular bedtime, meal times, exercise and consistent rules and expectations: *This is always an appropriate strategy for kids with ADHD, but is unlikely to resolve the issues Michael is having at his afterschool program, so is a great idea but insufficient.*

Thank you!

