

MEDICAL MEMO

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Medicines For ADHD - Updated Winter 2011

There are now about 22 FDA approved medicines for Attention Deficit Hyperactivity Disorder (ADHD) including the new Intuniv plus another handful of FDA unapproved options. The goal of this article is to make sense of these many choices and understand where the new Intuniv fits in. Medicine names are in bold below. Key concepts are in bold or underlined and are summed up at the end.

Choosing a medication for ADHD is done after becoming reasonably certain of the diagnosis and considering which, if any, treatment options are best for your child or you. Please see my detailed information packet about ADHD at <http://www.leeheyemd.com/>. It is also important to be clear what symptoms you want the ADHD medicine to help, what possible side effects you especially want to avoid, and if there are any convenience factors to consider. You and/or the youth must also **remember and accept that no medicine can do assignments, turn them in, or make good choices. These medicines can only assist one's efforts** - moderately usually, sometimes greatly.

ADHD medicines, especially the stimulants (see [Medications For ADHD](#)) and the non-stimulant Strattera, are most helpful for distractibility (short attention span, poor concentration, and lack of focus), for hyperactivity (can't sit still, restless, fidgety, excessive talking) and impulse control. Persons who have only the Inattentive (distractible) type of ADHD without any hyperactivity also respond well to stimulants and Strattera. Stimulants and Strattera are partially helpful for the common impulse control problems of acting or speaking without thinking first, blurting out, and butting into conversations, lines, games, and impulsive temper (Intuniv, guanfacine, clonidine, or imipramine may help this more). No ADHD medicines directly help organization problems (which is known as

Executive Functioning Disorder) or correct learning disorders like the various forms of reading and writing (dyslexia), math, or processing disorders. However, by helping any associated distractibility or hyperactivity, stimulants and Strattera can have partial to sometimes substantial indirect benefits for learning disorders and organization.

Since stimulants (also known as psychostimulants) and Strattera are usually the best medicines for ADHD let's next sort through them. Actually there are only 2 stimulant groups to consider. These are several forms of methylphenidate and of the amphetamines. (The most effective non-stimulant medicine for distractibility is Strattera and will be discussed after the stimulants.) So, really, this part is simpler than it looks. As you read on, be aware the ER, SR, CD, LA and XR suffixes all mean extended, slow, or longer duration forms of the basic medicine. Brand names are capitalized below while the generic chemical name is not.

Usually **side effects** can be avoided by conservative dosing and by fine tuning dose and form via close monitoring. Decreased appetite is the #1 side effect. If the dose is too strong or medicine is wrong speedy effects like delayed sleep onset, headache, stomach ache, tense muscles, dry mouth or irritability may occur. Or the opposite may occur - the person may feel too subdued, too calm, loose their spirit, spontaneity, spark, or seem "zombie" - like. Tics may occur especially in persons with a tendency toward them. Blood pressure or heart rate increases, skipped or irregular heart beats are possible though rarely significantly. All these are reversible by decreasing, changing, or stopping the medicine.

Methylphenidate (MPH for short) is the generic or chemical name of the medicine known by the brand names Ritalin, Ritalin SR, Methylin, Methylin ER, Metadate ER, Metadate CD, Ritalin LA, Concerta ER and Daytrana (a skin patch form of MPH). Thus,

these medicines all have the same basic ingredient. The main difference is how long they last and what mechanism is used to make it last longer. Generic forms, when available, are cheaper. **Focalin** (dexamethylphenidate) is the right handed isomer form of MPH which may give better duration and less "rebound" than MPH.

The **amphetamines** include Dexedrine (dextroamphetamine), Dexedrine spansules (SR), Adderall (generic known as "mixed amphetamine salts"), Adderall XR, and (the newest) Vyvanse (lisdexamfetamine). Adderall contains 50% dextroamphetamine and 50% of the very closely related isomer levo-amphetamine. The addition of levo-amphetamine gives Adderall its longer duration. Plain Adderall comes in a generic but Adderall XR does not yet. Vyvanse lasts longer, is often smoother and is less abusible.

Let's next discuss the relative merits and demerits of the MPH and amphetamine groups.

MPH (methylphenidate) is the gold standard that everything else is compared to; it's been studied the most. MPH is the mildest and it is cheap. It is a good place to start. Amphetamines are stronger, generally last a bit longer, can have more of a rough edge, and are more abusible. Some people do better on MPH products and some do better on the amphetamine options - there is no reliable way to tell which is better for you or your child without trying them.

Let's talk duration. Plain MPH (Ritalin, Methylin) lasts 3 to 4 hours, Focalin lasts 4 to 5 hours, Dexedrine lasts a good 4 hours, and plain Adderall 5 to maybe 6 hours. Each requires at least 2 doses to cover school hours while MPH and Dexedrine often require a third dose around 3 or 4 pm to also cover homework or work. Three doses a day (even two doses) can be a hassle leading to missed doses or lack of confidentiality due to having to take it at lunch at school or at day care after school, etc. Except for Strattera, the big growth of new ADHD medicine options is in new forms to extend the duration of existing medicines, not in creating new medicines to treat ADHD. Longer duration stimulant options are not only more convenient, they are also often smoother (less side effects and more consistent benefit through the day) and are less likely to cause the sometimes unpleasant

"rebound" as the medicine "wears off". There are now 5 ways companies have developed to increase the number of effective hours. First (and the oldest way), is to make a hard coated pill that dissolves slower - Ritalin SR and the generic MPH SR were made this way. In 2000 two companies came out with minor modifications of this MPH form and a new 10 mg size (as well as the generically priced 20 mg) - **Methylin ER** and **Metadate ER**. These last 6 to 8 hours usually. A second method to extend duration was brought out later in 2000 as **Concerta**, which uses a 3 layer OROS osmotic pressure release system to make plain MPH last 8 to 13 hours, usually 10 hours. In 2001 **Metadate CD** and **Ritalin LA** arrived as MPH based capsules containing pellets of 2 different release time targets which lasts about 8 hours. **Adderall XR** does the same with amphetamine and lasts closer to 10 hours. This capsule design containing time release pellets is the third method for making stimulants last longer. The fourth method came out in 2006 as the **Daytrana** transdermal system. This is a skin patch designed to be placed daily on one hip early each morning and removed about 9 hours later. The patch can thus avoid an oral dose and its duration can be changed by when you take off the patch. The fifth method appeared in 2007 as **Vyvanse** which is Dexedrine (dextroamphetamine) bonded to the amino acid lysine which results in a duration of 10 to 12 hours. This "pro-drug" (meaning pre or before) is not active until enzymes in the gastrointestinal tract or liver cut the lysine bond to free up the dextroamphetamine. This takes time and both results in extra duration of action and makes "snorting" or injecting it not worthwhile, thereby reducing abuse potential. The Daytrana skin patch (and less so Concerta) also reduce abusability.

Dexedrine (SR) "spansule" capsules were the first of the capsule strategy and typically last 6 to 8 hours. In late 2001 Adderall XR became available in its 2 pellet type capsule system to last 8 to 10 hours thereby avoiding need for a mid day dose at school or work. Concerta or Daytrana skin patch (with MPH) and Adderall XR or Vyvanse (with amphetamine) are the longest duration stimulant options. They may cover the whole day with only one morning dose. Focalin XR is next longest. Concerta, Adderall XR, Vyvanse, Metadate CD, Ritalin LA, Strattera, Focalin XR, and Daytrana are brands costing over \$3 a day and may be a high co-pay choice or are not covered

on some insurance formularies. Some patients will still require a dose of regular MPH or amphetamine around 4 PM to cover the rest of the day. **Cylert** (pemoline) is an effective, truly once a day non-abusable stimulant option that is little used since it has about a 1 in 10,000 risk of unpredictable severe liver damage or failure.

Preparation types available thus include tablets both short and longer duration (MPH, Focalin, Adderall, Methylin ER, Metadate ER, Ritalin SR, MPH SR), capsules that release 50% quickly and 50% in about 4 hours (Focalin XR, Ritalin LA, Dexedine Spansules, Adderall XR - all of which can be sprinkled on food to ease swallowing; Metadate CD does the same except it releases 30% immediately and 70% later), the Concerta 3 layer techno pill, capsules not designed for splitting (Vyvanse and Strattera are also not good for splitting), and the Daytrana skin patch. **Methylin** also makes a liquid dose form that lasts up to 4 hours for situations where a liquid is preferred. All Methylin forms contain no dyes.

[Page 2 of my ADHD Medication chart](#) shows **non stimulant medicines that may help ADHD.**

Strattera (atomoxetine) is the FDA approved (early 2003) non stimulant ADHD medicine that may rival the stimulants for at least some persons in helping distractibility (attention, concentration, focus) and perhaps hyperactivity and impulsivity. It works via norepinephrine reuptake inhibition (NRI) to increase primarily norepinephrine in the brain but has little effect on dopamine. Stimulants increase both these neurotransmitters but in a different way. Thus, Strattera helps ADHD while often causing less appetite suppression, sleep disturbance, rebound, irritability, tics, or other stimulant side effects. Strattera is not abusable. As a convenience plus, Strattera can be called in, refills can be written, and there is no need for handwritten prescriptions like all stimulants need. Strattera works to increase norepinephrine (NRI) in a way similar to how the antidepressants Prozac, Zoloft, Paxil, Luvox, Celexa, and Lexapro increase serotonin (SRI). Strattera may occasionally have some antidepressant or, more often, anxiety benefit. Strattera must be taken 7 days a week to give a smooth and effective level in the body and must build up for 2 to 4 weeks before it is fully effective. In contrast, stimulants can be given when needed

and work for a certain number of hours and then are gone. The potential advantage to the steady blood level effect of Strattera is that it should be present and working 24 hours a day - even on awakening before the morning dose is taken and late into the evening when stimulants have usually worn off. Because of this slow build up effect it may be better when changing from a stimulant to Strattera to overlap both meds the first few weeks. For some patients it may be helpful to take a stimulant and Strattera (or other non stimulant medicine) at the same time on an ongoing basis. In addition to a usually milder and less frequent group of possible stimulant like side effects, Strattera may bother the stomach by causing nausea, or cause sleepiness. Taking it with food, switching the medicine to evening, or giving half in the am and half in the pm may work better. Strattera comes in capsules of several strengths, is usually started in the morning, and the dosage increases with body weight. Response may be better if the dose is set at the higher end of the recommended range although some people respond and tolerate it better at low doses. Two to four weeks should be given to gauge response. Studies and clinical experience show that some people respond better to Strattera than a stimulant or vice versa. If one doesn't work well the other may still help.

Other options on page 2 of my ADHD medication chart are less helpful for attention, concentration, focus, and distractibility than Strattera and the stimulants but may have other advantages. These medicines include the antidepressants Wellbutrin (bupropion) and imipramine (as well as its cousins). Generally, if I am trying to mainly treat ADHD, especially distractibility and inattention, I will use a stimulant or possibly Strattera first for that and then add an antidepressant or anti anxiety medicine if depression or anxiety are also present.

Tenex (guanfacine), Intuniv (guanfacine ER) or clonidine are not usually as helpful for distractibility and inattention as the stimulants are but are just as good or better for hyperactivity and impulsivity. They also don't cut appetite and do suppress tics (which stimulants may precipitate or worsen). They are given 2 or 3 times a day. With guanfacine lunch dosing can often be avoided. **Intuniv** is a good new (2009) extended release guanfacine that allows once a day dosing (usually am), less sedation, smoother

effect, plus all the other advantages of guanfacine or clonidine. This family of central nervous system calmers also often help sleep, reduce the "hyperarousal" symptoms of Post Traumatic Stress Disorder (PTSD), and opiate (pain killers) and nicotine withdrawal.

The other nonstimulants in this paragraph are infrequently used options. **Amantadine** is a generic (Symmetrel is the brand name) that increases primarily dopamine and not norepinephrine. Thus some patients respond better to its similar but more limited actions. Amantadine (and its cousin rimantadine) is mainly used to treat parkinsonism of various types and also prevents and treats Influenza type A (not B). Amantadine comes as a capsule or liquid without much dose adjusting possible except via the liquid and is usually given twice a day for ADHD. (Two brand name and more pure dopamine agonists, **Mirapex** or **Requip**, could also be tried.) **Provigil** (modafinil) was approved by the FDA in 2000 for "excessive daytime sleepiness" caused by certain sleep disorders like sleep apnea and narcolepsy. Neither it or amantadine are approved by the FDA for ADHD although doctors may use them for ADHD. There are only a few studies so far showing that amantadine or Provigil helps ADHD.

Provigil (and its even longer duration isomer armodafinil known as Nuvigil) is only available as an expensive brand. It comes as a tablet given once a day in the morning. Although it is similar to other stimulants in several ways it also has differences that make it an alternative when other stimulants fail or aren't tolerated. All stimulants except Cylert may be abused but the non-stimulants Intuniv, guanfacine, and Strattera are not abusible which gives another reason to consider these options in certain situations. **The top three abused substances (plus nicotine) in middle school through college are now alcohol, marijuana, and Adderall.**

To summarize, despite the growing number of medicines for ADHD, stimulants remain generally the first choice. Strattera is a non-stimulant attention span boosting option. Intuniv, guanfacine, and clonidine have their very useful niche as well. Almost all the other "new" medicines are just extended duration, brand name (costlier) versions of the big two: methylphenidate (Ritalin) and amphetamine (Adderall). These new options do often, but not always, bring benefits that outweigh their extra monetary cost. There remain a few non stimulant older options and a few atypical stimulant choices to consider mainly as back-up plans.

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