

## **APPROPRIATE TREATMENT OF ATTENTION DEFICIT HYPERACTIVITY DISORDER**

### *Background*

Although a variety of social and behavioral modifications are employed in the treatment of attention deficit/hyperactivity disorder (ADHD), drug therapy continues to be a mainstay. Until November 2002, agents in the CNS stimulant class were the only drugs FDA-approved for the treatment of ADHD and these agents remain first-line therapy.

**Several well-controlled trials in children with uncomplicated ADHD have established the efficacy of stimulants with response rates reaching 60 to 75% in stimulant naive patients with placebo response rates ranging from zero to 30%. Furthermore, it has been demonstrated that a trial of an alternative stimulant after initial failure may push response rates up to 80 to 90%. Combination therapy has not been adequately described in the literature.**

### *Comparison of ADHD agents*

Brand*	Generic	Dose/Schedule	Duration	Average Cost**	
				Brand	Generic
Ritalin	Methylphenidate short-acting	5-20mg BID-TID	3-5 hrs	\$41.35	\$25.34
Ritalin SR	Methylphenidate intermediate-acting	20-40mg QD-BID	3-8 hrs	\$46.18	\$33.59
Concerta; Metadate CD; Ritalin LA	Methylphenidate long-acting	18-72 mg QD	8-12 hrs	\$84.90	N/A
Focalin	Dexmethylphenidate	2.5-10mg BID-TID	3-5 hrs	\$54.79	N/A
Dextrostat	Dextroamphetamine short-acting	5-15mg BID-TID	4-6 hrs	\$64.84	\$28.72
Dexedrine spansule	Dextroamphetamine intermediate-acting	5-15mg QD-BID	6-8 hrs	\$47.84	\$36.62
Adderall	Dextroamphetamine/ Amphetamine intermediate-acting	5-30mg QD-BID	6-8 hrs	\$97.84	\$85.71
Adderall XR	Dextroamphetamine/ Amphetamine long-acting	10-30mg QD	8-12 hrs	\$98.88	N/A
Strattera	Atomoxetine	20-40mg QD-BID	12-24 hrs	\$93.99	N/A

\* Brand names provided for reference; Idaho Medicaid requires generic unless documented "medically necessary"

\*\* Cost based on AWP for one month of therapy

### *Drug therapy for ADHD*

The common stimulants used in ADHD include methylphenidate, dextroamphetamine, and mixed amphetamine salts. Pemoline (Cylert<sup>®</sup>) is considered a second-line agent due to its propensity to induce hepatotoxicity.

Other second-line agents include tricyclic antidepressants, bupropion, clonidine, and Strattera<sup>®</sup> (atomoxetine). Evidence of efficacy in ADHD for most of these agents is inferior to that of the stimulants. Strattera<sup>®</sup> has received much attention since its release into the U.S. market. It is a non-cyclic, non-stimulant, norepinephrine reuptake inhibitor that has demonstrated clinical efficacy for controlling the core symptoms of ADHD in four well-controlled trials with good tolerability. **One open-label trial has suggested that the efficacy of Strattera<sup>®</sup> may approach that of stimulants, although no large head-to-head trials have been conducted to date. Also of note, Strattera<sup>®</sup> has not yet been studied in combination with stimulants for ADHD refractory to stimulants alone.**

### *ADHD drug therapy in Idaho*

**Files from the medicaid claims database indicate that stimulant and Strattera<sup>®</sup> therapy cost the state of Idaho \$3.4 million in 2003, which was more than double the amount spent in 2001. Evidence from the database also suggests that dosing guidelines for long-acting stimulants are not always followed (up to 20% of patients are dosed more frequently than QD) and combination therapy with multiple stimulants is common.** Furthermore, drugs with antagonistic effects to stimulant therapy (such as CNS depressants) are also prescribed for ADHD patients.

### *Recommendations*

Current guidelines recommend both non-pharmacologic therapies as well as drug treatments for ADHD. **Research to date has not shown clear advantages of one stimulant over another, but titration to the highest recommended dose of one agent should be attempted before trying another. Because evidence is lacking at this time, the use of two or more ADHD medications in combination is discouraged. Also, duration of activity should be taken into account when prescribing stimulants, with particular attention paid to single daily dosing of agents considered to be long-acting.** The appropriate use of stimulant medications in the treatment of ADHD will result in improved patient care and important economic savings.

### *References*

1. American Academy of Pediatrics Subcommittee on Attention-Deficit/Hyperactivity Disorder and Committee on Quality Improvement. Clinical Practice Guideline: Treatment of the School-Aged Child With Attention-Deficit/Hyperactivity Disorder. *Pediatrics* 2001;108(4):1033-1044.
2. Dimpson D and Perry CM. Atomoxetine. *Pediatr Drugs* 2003;5(6):407-415
3. Olfson M, Gomeroff MJ, Marcus SC, and Jensen PS. National trends in the treatment of attention deficit hyperactivity disorder. *Am J Psychiatry* 2003;160:1071-1077.
4. Pliska SR. Non-stimulant treatment of attention-deficit/hyperactivity disorder. *CNS Spectrums* 2003;8(4):253-258.