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ANOTHER LONG-ACTING METHYLPHENIDATE (*METADATE CD*)

Methylphenidate is now available in a new extended-release formulation (*Metadate CD* – Celltech) for treatment of attention deficit/hyperactivity disorder (ADHD). The new product, which is a Schedule II controlled substance, is being advertised directly to consumers.

SOME STIMULANT DRUGS FOR ADHD

Drug	Typical pediatric dosage	Cost*
Methylphenidate		
short duration	20 mg bid (or 10 mg tid)	
generic price (Geneva)		\$ 42.86
<i>Ritalin</i> (Novartis)		53.48
long duration		
generic (Geneva)	40 mg in AM	66.57
<i>Metadate ER</i> (Celltech)		63.60
<i>Methylin ER</i> (Mallinckrodt)		67.17
<i>Ritalin SR</i> (Novartis)		83.05
<i>Metadate CD</i> (Celltech)		69.36
<i>Concerta</i> (Alza)	36 mg in AM	73.13
Dextroamphetamine		
generic (Barr)	10 mg bid (or 5 mg tid)	33.64
<i>Dexedrine</i> (GlaxoSmithKline)		38.80
long duration		
<i>Dexedrine Spansules</i> (GlaxoSmithKline)	20 mg in AM	57.76
Amphetamine mixture		
<i>Adderall</i> (Shire US)	10 mg bid, 5 hours apart	80.91

* Cost for 30 days' treatment, according to AWP listings in *Drug Topics Red Book Update*, September 2001.

PHARMACOKINETICS – The new *Metadate CD* capsule contains both immediate-release (IR) and extended-release coated beads; 30% of the dose is provided by the IR component and 70% by extended release. Plasma concentrations peak twice, first at 1.5 hours like IR methylphenidate, and then again at 4.5 hours. Taken once daily, it produces serum concentrations similar to those with IR methylphenidate b.i.d.

CLINICAL TRIALS – No clinical trials with the new formulation have been published. An unpublished double-blind 3-week trial in 321 children with ADHD, presented to the FDA, found *Metadate CD* capsules given once daily in the morning at a dose of 20 to 60 mg more effective than placebo in reducing ADHD symptoms at 10 AM and 2 PM. *Metadate CD* has had, according to Medical Letter consultants, about an 8-hour duration of action, somewhat shorter than the 12-hour duration of *Concerta* (WE Pelham et al, *Pediatrics* 2001; 107:e105; M Wolraich et al, *Pediatrics* 2001; 108:883).

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ADVERSE EFFECTS — As with other methylphenidate formulations, anorexia, insomnia, headache and abdominal pain have been reported with the new product. Some children who take long-acting preparations may suffer from loss of appetite for the evening meal or insomnia, but insomnia can also be caused by ADHD itself.

DOSAGE — *Metadate CD* is available only in 20-mg capsules. The manufacturer recommends starting with 20 mg once daily in the morning. Dosage can be increased to a maximum of 60 mg daily in 20-mg increments once weekly. Patients already taking 10 mg of immediate-release methylphenidate b.i.d. should start with 20 mg once daily; those taking 20 mg b.i.d. should start with 40 mg.

AMPHETAMINE ALTERNATIVES — Dextroamphetamine is as effective as methylphenidate in children with ADHD and has about a 5-hour duration of action. Some children unresponsive or intolerant to methylphenidate have tolerated or responded well to dextroamphetamine, and vice versa (J Elia et al, *Psychiatry Res* 1991; 36:141). *Adderall*, which is a mixture of amphetamines, is similar to dextroamphetamine, but has a shorter duration of action than *Dexedrine Spansules*; a sustained-release formulation (*Adderall XR*) will probably be available soon.

CONCLUSION — *Metadate CD* extended-release methylphenidate capsules have a rapid onset and apparently continue to act throughout the school day, but not as long as *Concerta*. The shorter duration might be an advantage for children with loss of appetite at suppertime or difficulty falling asleep due to medication, but possibly a disadvantage for those who need the drug in the late afternoon. Comparative trials are needed, not only with *Concerta*, but also with other methylphenidate formulations.

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