

New Drug Bulletin:

Methylphenidate Transdermal System (Daytrana™ - Shire Pharmaceuticals)

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Methylphenidate transdermal system (Daytrana™) received FDA approval on April 4, 2006 and is the first methylphenidate patch for the treatment of Attention-Deficit/Hyperactivity Disorder (ADHD) in children ages 6-12 years old. Methylphenidate is a central nervous system (CNS) stimulant thought to inhibit the reuptake of norepinephrine and dopamine presynaptically, and enhance the release of catecholamines into the synaptic cleft.

Serum concentrations of d-methylphenidate after a single application of the patch are similar to those achieved with a single dose of once-daily oral methylphenidate formulations. Time to peak serum concentrations ranges from 7.1-8.8 hours. After multiple applications, serum concentrations are up to 1.9 times higher than those found with oral formulations, indicating that absorption of methylphenidate increases with continued use. Methylphenidate is highly lipophilic and 10-33% protein-bound, giving it the ability to efficiently penetrate the CNS. Methylphenidate is metabolized by de-esterification to the inactive metabolite α -phenyl-piperidine acetic acid (ritalinic acid), which is excreted in the urine. The mean elimination half-life is 3-4 hours.

Two randomized double-blind, placebo-controlled trials demonstrated the efficacy of the Daytrana™ in children aged 6 to 12 years old. Mean changes from baseline in both the SKAMP-D scale and the ADHD-Rating Scale-IV showed statistically significant improvements in children receiving Daytrana™ compared to placebo. There are no data for the use of Daytrana™ in the treatment of adults with ADHD.

The most common adverse effects associated with Daytrana™ are decreased appetite (26%), insomnia (13%), nausea and vomiting (10-12%), weight loss (9%), tic (7%), affect lability (6%), and nasal congestion or nasopharyngitis (5-6%). Early removal minimizes late day side effects such as insomnia or decreased appetite. Application site irritation (erythema) and contact sensitization (intense local reaction with edema, papules, or vesicles) are possible with the use of the patch, but incidence is low when applied for 9 hours per day, alternating right and left hip areas.

Methylphenidate inhibits the metabolism of warfarin, phenytoin, phenobarbital, primidone, tricyclic antidepressants, and selective serotonin reuptake inhibitors. Patients taking these medications concurrently may need dose adjustments. Because methylphenidate can increase blood pressure, it may decrease the efficacy of antihypertensive medications. Methylphenidate is contraindicated with monoamine oxidase inhibitor therapy. It is also contraindicated with agitation, glaucoma, tics or family history of Tourette's syndrome, and hypersensitivity to methylphenidate.

Apply the patch to the hip area once daily in the morning 2 hours prior to needed effect and remove after a maximum of 9 hours. Alternate between the right and left sides to avoid irritation. If the patch falls off, place a new patch on a different area of the same hip, but total

wear time should not exceed 9 hours from application of the first patch. The patch is applied for a total of 9 hours, but effects last at least 12 hours. Absorption increases with external heat (such as a heating pad, electric blanket, or heated water-bed) or when patch is applied to inflamed skin. The patches must not be cut as the effects on dose delivery have not been studied. Initiate treatment at the lowest patch dose, 10 mg, and titrate to effect on a weekly basis in both methylphenidate-naïve patients and when converting patients from oral methylphenidate agents regardless of previous dose. After removal, fold the patch so that no adhesive is exposed and flush or place in a lidded container.

Daytrana™ is supplied in 10mg, 15 mg, 20 mg, and 30 mg patches and comes in trays of 10 or 30. Store unused patches in their original pouch at room temperature. Use patches within 2 months of opening the tray.

Table 1. Cost Comparison of Once-Daily Methylphenidate Formulations

	Starting Dose	AWP 30-day supply	WAC 30-day supply
Daytrana™ (10 mg, 15 mg, 20 mg, 30 mg)	10 mg once daily	198.50	119.40
Concerta® (18 mg, 27 mg, 36 mg, 54 mg)	18 mg once daily	111.95	89.56
Ritalin LA® (10 mg, 20 mg, 30 mg, 40 mg)	20 mg once daily	92.69	74.15
Metadate CD™ (10 mg, 20 mg, 30 mg)	20 mg once daily	82.29	65.83

In summary, Daytrana™ is the first methylphenidate transdermal system to be approved for the treatment of ADHD in children ages 6-12 years old. Benefits of the patch include its once daily application, the ability to remove the patch early to minimize side effects, and its availability for children who are unwilling or unable to take oral medications. Due to risks of allergic contact dermatitis and methylphenidate sensitivity, it may not be first-line treatment, but will be available for patients unable or unwilling to take methylphenidate orally.

1. Daytrana™ (methylphenidate transdermal system) [package insert]. Wayne, PA: Shire Pharmaceuticals Ireland Limited, April 2006.
2. Anderson VR, Scott LJ. Methylphenidate transdermal system: in attention-deficit hyperactivity disorder in children. *Drugs* 2006;66(8):1117-26.
3. Fleming T. ed 2005 Redbook. Montvale, NJ: Thomson PDR; 2005.

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