



Therapeutic Class ReviewSM

methylphenidate transdermal system (DaytranaTM) dexamethylphenidate extended-release (Focalin XRTM)

September 2006

New Products for Review:

methylphenidate transdermal system
(DaytranaTM) [Shire]

Dossier Provided by Manufacturer: No

Dossier Evaluation: 1

dexamethylphenidate extended-release
(FocalinTM XR) [Novartis]

Dossier Provided by Manufacturer: Yes

Dossier Evaluation: 1

1- dossier w/missing components

2- all components present, except pharmacoeconomic model

3- all components present (comprehensive)

Executive Summary

Methylphenidate transdermal system (Daytrana)

- Methylphenidate transdermal system (Daytrana) is an adhesive-based matrix transdermal system (patch) that is applied to intact skin.
- Clinical trials are limited to children 6 years to 12 years of age, and were limited to “simulated classroom” studies.
- There are several concerns with the methylphenidate transdermal system (Daytrana):
 - Methylphenidate transdermal system (Daytrana) is applied daily two hours before its effect is needed, then is removed 9 hours after application.
 - Medication continues to be absorbed from the patch if not removed after 9 hours.
 - Original application to the FDA was for a 12 hour application time. That application was rejected due (in part) to the high rate of adverse reactions.
 - Although parents “had no trouble” remembering to remove the patch on time during the trial, there is uncertainty about compliance of patch removal when used in “real world” circumstances.

Dexamethylphenidate extended-release (Focalin XR)

- Dexamethylphenidate extended-release (Focalin XR) is indicated for the treatment of the symptoms of ADHD in both children and adults.

- Dexmethylphenidate is the active racemate of methylphenidate. Approximately one-half the milligram dose of dexmethylphenidate is needed to achieve an equivalent effect to methylphenidate.
- Dexmethylphenidate extended-release (Focalin XR) is a long-acting formulation of dexmethylphenidate that releases medication in two phases, using a proprietary SODAS® (Spheroidal Oral Drug Absorption System) technology.
 - Fifty percent of medication is released as “immediate-release”.
 - The remainder is absorbed over the next 12 to 16 hours.

Evidence

Methylphenidate transdermal system (Daytrana) / dexmethylphenidate ER (Focalin XR)

	Methylphenidate transdermal System (Daytrana)	Dexmethylphenidate ER (Focalin XR)
Evidence in ADHD:		
Children	No useful evidence	No useful evidence
Adults	No evidence	No useful evidence

• ***Considerations in Subpopulations:***

	Methylphenidate transdermal system (Daytrana)²	Dexmethylphenidate extended-release (Focalin XR)³
Geriatrics	Safety and efficacy have not been established in patients older than 12 years.	Safety and efficacy have not been established in patients older than 60 years.
Pediatrics	Safety and efficacy in children under 6 years old have not been established. Long-term effects of methylphenidate in children have not been well established	Safety and efficacy in children under 6 years old have not been established. Long-term effects of dexmethylphenidate in children have not been well established
Race/Ethnicity	The influence of race on the pharmacokinetics of methylphenidate after administration of methylphenidate transdermal system (Daytrana) has not been defined.	There is insufficient experience with the use of dexmethylphenidate extended-release (Focalin XR) to detect ethnic variations in pharmacokinetics.
Gender	The pharmacokinetics of methylphenidate after single and repeated doses of methylphenidate transdermal system (Daytrana) were similar between boys and girls with ADHD, after allowance for	After administration of dexmethylphenidate extended-release (Focalin XR) the first peak, (C _{max1}), was on average 45% higher in women. Pharmacokinetic parameters for dexmethylphenidate after Focalin

	differences in body weight.	immediate-release tablets were similar for boys and girls.
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Decision

- Methylphenidate transdermal system (Daytrana) is non-preferred/non-formulary because:
 - There is no useful evidence that methylphenidate transdermal system (Daytrana) is safer or more efficacious than existing preferred/formulary alternatives.
 - There are unresolved concerns regarding the safety of methylphenidate transdermal system (Daytrana).
 - Methylphenidate transdermal system (Daytrana) costs more than existing formulary alternatives, without providing additional clinical benefit.
- Dexmethylphenidate extended-release (Focalin XR) is non-preferred/non-formulary because:
 - There is no useful evidence that dexmethylphenidate extended-release (Focalin XR) is safer or more efficacious than existing preferred/formulary alternatives.

Products

Drug Products ¹⁻³	FDA approval ^a	FDA approved indications	Usual Dose/Route	Potential Off-label Uses ^c
dexmethylphenidate Focalin [®] Focalin XR [®]	11/2001 05/2005	- ADHD	5mg PO BID 10mg PO QD	- none listed – likely similar to methylphenidate
methylphenidate Methylin [®] Ritalin [®]	04/2003 12/1955	- ADHD - Narcolepsy	10mg PO BID	- autism - bipolar disorder: adjunct - bulimia nervosa - cancer – fatigue, depression, pain, brain tumors - cerebral palsy – adjunct - cocaine dependence - dementia - depression - epilepsy - fatigue - hiccoughs, intractable - impaired cognition - paraphillia – adjunct - schizophrenia - traumatic brain injury
methylphenidate extended release tablets Metadate ER Methylin ER Ritalin SR [®] Concerta [®]	10/1999 05/2000 03/1982 08/2000	- ADHD - Narcolepsy (except for Concerta)	40mg PO QD 36mg PO QD	
methylphenidate extended release capsules Metadate CD [®] Ritalin LA [®]	04/2001 06/2002	- ADHD	40mg PO QD	
methylphenidate transdermal system Daytrana [®]	04/2006	- ADHD	10mg – 30mg / 9 hrs QD	
amphetamine salt combo Adderall [®]	01/1960	- ADHD - Narcolepsy	10mg PO BID	- cerebrovascular accident - hiccoughs
amphetamine salt combo extended release Adderall XR [®]	10/2001	- ADHD - Narcolepsy	15mg PO QD	
dextroamphetamine (Dexadrine [®] , Dextrostat [®])	05/1975	- ADHD - Narcolepsy	10mg PO BID	- cocaine dependence - depression - mania - schizophrenia - sleep deprivation
dextroamphetamine sustained release Dexadrine Spansules	08/1976	- ADHD - Narcolepsy	20mg PO QD	
methamphetamine Desoxyn [®]	12/1943	- ADHD - Exogenous Obesity	10mg PO BID	- none listed
atomoxetine Strattera [®]	11/2002	- ADHD	80mg PO QD	- nocturnal enuresis

^a Date applies to approval date for the original brand name medication where there are now generics available.

^c As listed in © 1974 - 2005 Thomson MICROMEDEX database or as referenced.

ADHD = Attention deficit disorders/Attention deficit hyperactivity disorder, QD = once daily, BID = twice daily

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