



## Therapeutic Class Review<sup>SM</sup>

### Behavior Modification – lisdexamfetamine (Vyvanse<sup>TM</sup>)

May 2008

#### New Product for Review:

Lisdexamfetamine (Vyvanse<sup>TM</sup>) [Shire]

#### Dossier Provided by Manufacturer:

##### Dossier Evaluation: 2

- 1- dossier w/missing components
- 2- all components present, except pharmacoeconomic model
- 3- all components present (comprehensive)

#### Executive Summary

- Lisdexamfetamine (Vyvanse) is a pro-drug of dextroamphetamine. Lisdexamfetamine (Vyvanse) has no demonstrable activity in either *in vitro* assays or *in vivo* animal data. <sup>[2,12]</sup>
- After oral administration, lisdexamfetamine (Vyvanse) is rapidly absorbed from the gastrointestinal tract and converted to dextroamphetamine, which is responsible for the drug's activity. <sup>[2,12]</sup>
- In their clinical review for approval, the FDA noted the small number of patients exposed to lisdexamfetamine (Vyvanse) during the development program (n=272). <sup>[2,12]</sup>
  - The FDA considers lisdexamfetamine (Vyvanse) to be a prodrug for d-amphetamine, a compound which has a substantial safety history.
  - Approval was based on superior efficacy compared to placebo in the two randomized controlled trials (RCTs).
- Based on submitted pharmacokinetic trials, the FDA assessed lisdexamfetamine (Vyvanse) to have a similar time-concentration profile to amphetamine/dextroamphetamine SR (Adderall XR). <sup>[2,12]</sup>
  - The AUC and C<sub>max</sub> for d-amphetamine from 75 mg of lisdexamfetamine (Vyvanse) was comparable to both d-amphetamine and l-amphetamine from 35 mg of amphetamine/dextroamphetamine SR (Adderall XR).
  - There has been no trials to help correlate differences in pharmacokinetic profiles with improved clinical effects.
- Both the FDA and DEA were unconvinced that lisdexamfetamine (Vyvanse) had lower abuse potential due to similarity to d-amphetamine in: <sup>[2,13]</sup>
  - Pharmacokinetic and adverse event profiles.
  - Similar “rewarding” effects.
  - Psychological dependence and tolerance.

- Adderall XR and Metadate CD were added as preferred/formulary due to similar practical considerations of offering preferred/formulary options for long-acting stimulants and the positive financial impact on both patients and plans.
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## Evidence

- There is no useful evidence to show an advantage of lisdexamfetamine (Vyvanse) over existing preferred/formulary treatment options for the management of patients with ADHD.
  - Efficacy and safety appears to be similar to dextroamphetamine.
  - Despite claims of reduced abuse potential, lisdexamfetamine (Vyvanse) was designated a schedule II controlled substance by the DEA, and no useful evidence was found to support a claim of reduced abuse potential.

## Decision

Add Vyvanse as preferred/formulary because:

- Efficacy and safety appear to be similar to dextroamphetamine.
- It provides choice for prescribers and members.
- It lowers overall net cost for the ADHD class.

## Products

Drug Products <sup>1-3</sup>	FDA approval <sup>a</sup>	Patent Expiration(s) <sup>c</sup>	FDA approved indications	Usual Dose/Route	Potential Off-label Uses <sup>c</sup>
dexamethylphenidate Focalin <sup>®</sup> Focalin XR <sup>®</sup>	11/2001 05/2005	12/2015 12/2019	- ADHD	5 mg PO BID 10 mg PO QD	- none listed – likely similar to methylphenidate
methylphenidate Methylin <sup>®</sup> Ritalin <sup>®</sup>	04/2003 12/1955		- ADHD - Narcolepsy	10 mg PO BID	- autism - bipolar disorder: adjunct - bulimia nervosa - cancer – fatigue, depression, pain, brain tumors - cerebral palsy – adjunct
methylphenidate extended release tablets Metadate ER Methylin ER Ritalin SR <sup>®</sup> Concerta <sup>®</sup>	10/1999 05/2000 03/1982 08/2000	04/2008	- ADHD - Narcolepsy (except for Concerta)	40 mg PO QD  36 mg PO QD	- cocaine dependence - dementia - depression - epilepsy - fatigue - hiccoughs, intractable - impaired cognition - paraphilia – adjunct - schizophrenia - traumatic brain injury
methylphenidate extended release capsules Metadate CD <sup>®</sup> Ritalin LA <sup>®</sup>	04/2001 06/2002	10/2020 11/2019	- ADHD	40 mg PO QD	
methylphenidate transdermal system Daytrana <sup>®</sup>	04/2006	9/2018	- ADHD	10 mg – 30 mg / 9 hrs QD	
amphetamine salt combo Adderall <sup>®</sup>	01/1960	N/A	- ADHD - Narcolepsy	10 mg PO BID	- cerebrovascular accident - hiccoughs
amphetamine salt combo extended release Adderall XR <sup>®</sup>	10/2001	01/2009	- ADHD - Narcolepsy	10 mg to 30 mg PO QD	
dextroamphetamine (Dexedrine <sup>®</sup> , Dextrostat <sup>®</sup> )	05/1975	N/A	- ADHD - Narcolepsy	10 mg PO BID	- cocaine dependence - depression - mania - schizophrenia - sleep deprivation
dextroamphetamine sustained release			- ADHD - Narcolepsy	20 mg PO QD	

Dexedrine Spansules	08/1976	N/A			
methamphetamine Desoxyn <sup>®</sup>	12/1943	N/A	- ADHD - Exogenous Obesity	10 mg PO BID	- none listed
atomoxetine Strattera <sup>®</sup>	11/2002	11/2016	- ADHD	80 mg PO QD	- nocturnal enuresis
lisdexamfetamine Vyvanse <sup>®</sup>	6/2023		- ADHD	30 mg to 70 mg PO QD	- none listed

<sup>a</sup> Date applies to approval date for the original brand name medication where there are now generics available.

<sup>c</sup> 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

## References

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