

Focalin[®] XR
(dexamethylphenidate HCl)
Extended-Release Capsules CII

Treatment for Adults With ADHD

ADHD in Adults Is Prevalent and Under-recognized

- ADHD affects approximately 3% to 6% of children [Goldman et al. 1998, p.1100A] ¹
- Persistence into adulthood occurs in 46%-66% of children [Barkley et al. 2002, p.288A] ²
 - Based on pediatric persistence rate of up to 65%, 2% – 7% of all adults have ADHD³ [Dulcan et al. 1997, p.1A]
- Large epidemiologic study of 9,282 adults in the US found that 4.4% of adults met full criteria for persistent childhood onset of ADHD⁴ [Kessler et al 2006, p. 716ABC]
- However, ADHD is still under-recognized and under-diagnosed in adults^{2,3,5} [Barkley et al. 2002, p.10A] [Weiss et al. 2004, p.27A] [Dulcan et al. 1997, p.24A]

1. Goldman LS et al. *JAMA*. 1998;279:1100-1107. 2. Barkley RA et al. *J Abnormal Psych*. 2002;111:279-289. 3. Dulcan M et al. *J Am Acad Child Adolesc Psychiatry*. 1997;36(suppl 10):85S-121S. 4. Kessler et al. In Press *AJP*. 2006. 5. Weiss MD, and Weiss JR. *J Clin Psychiatry*. 2004;65:27-37.

DSM-IV Core Symptoms of ADHD in Adults *[Weiss et al. 2003, p.717 A]*

Inattention

- Makes careless mistakes
- Is inattentive to tasks
- Has difficulty following verbal instructions
- Has difficulty completing tasks
- Is disorganized
- Avoids tasks that require much concentration
- Misplaces things
- Is easily distracted
- Is forgetful

Hyperactivity/Impulsivity

- Fidgets with hands or feet
- Has trouble sitting still
- Feels restless and jittery
- Has trouble doing things quietly
- Is always “on the go”
- Talks excessively
- Acts before thinking things through
- Is Impatient
- Interrupts others

ADHD Presents Differently in Adults Than in Children

- ADHD behaviors change with age
 - Adults tend to be less hyperactive than children [*Weiss et al. 2004, p.28A*]
 - The male to female ratio narrows [*Weiss et al. 2004, p.29A*]
- Different diagnostic challenges
 - Relationship to comorbid disorders
 - Often present with symptoms of anxiety or depression [*Weiss et al. 2003, p.716B*]
- Patients have lived with symptoms and may learn to compensate for some of them [*Weiss et al. 2004, p.28B*]

Lifetime Course of ADHD

Symptoms: Inattention Domain

[APA DSMV-IV 2000 p. 89A; Weiss 2004 p. 27D, 28C,D]

Childhood

Difficulty sustaining attention

Doesn't listen

No follow through

Can't organize

Loses important items

Adult

Difficulty sustaining attention
(meetings, reading, paperwork)

Paralyzing procrastination

Slow, inefficient

Poor time management

Disorganized

Lifetime Course of ADHD Symptoms: Hyperactivity/Impulsivity Domain

[APA DSMV-IV 2000 p. 86A; Weiss 2004 p.28 A,C,F,H]

Childhood

Squirming, fidgeting
Can't stay seated
Can't wait turn
Runs/climbs excessively
Can't play/work quietly
On the go/driven by motor
Talks excessively
Blurts out answers
Intrudes/interrupts others

Adult

Inefficiencies at work
Can't sit through meetings
Can't wait in line
Drives too fast
Self-selects very active job
Can't tolerate frustration
Talks excessively
Makes inappropriate comments
Interrupts others

Potential Impact of Untreated ADHD Across the Lifespan [AAP 2000 pg. 1158 C; Barkley et al. 2002, p.10 B, 13 A-D; Baren 2002, pg. 3A]

Low self-esteem

Academic limitations

Smoking and substance abuse

Legal problems



Childhood

Adolescence

Adulthood

Injuries

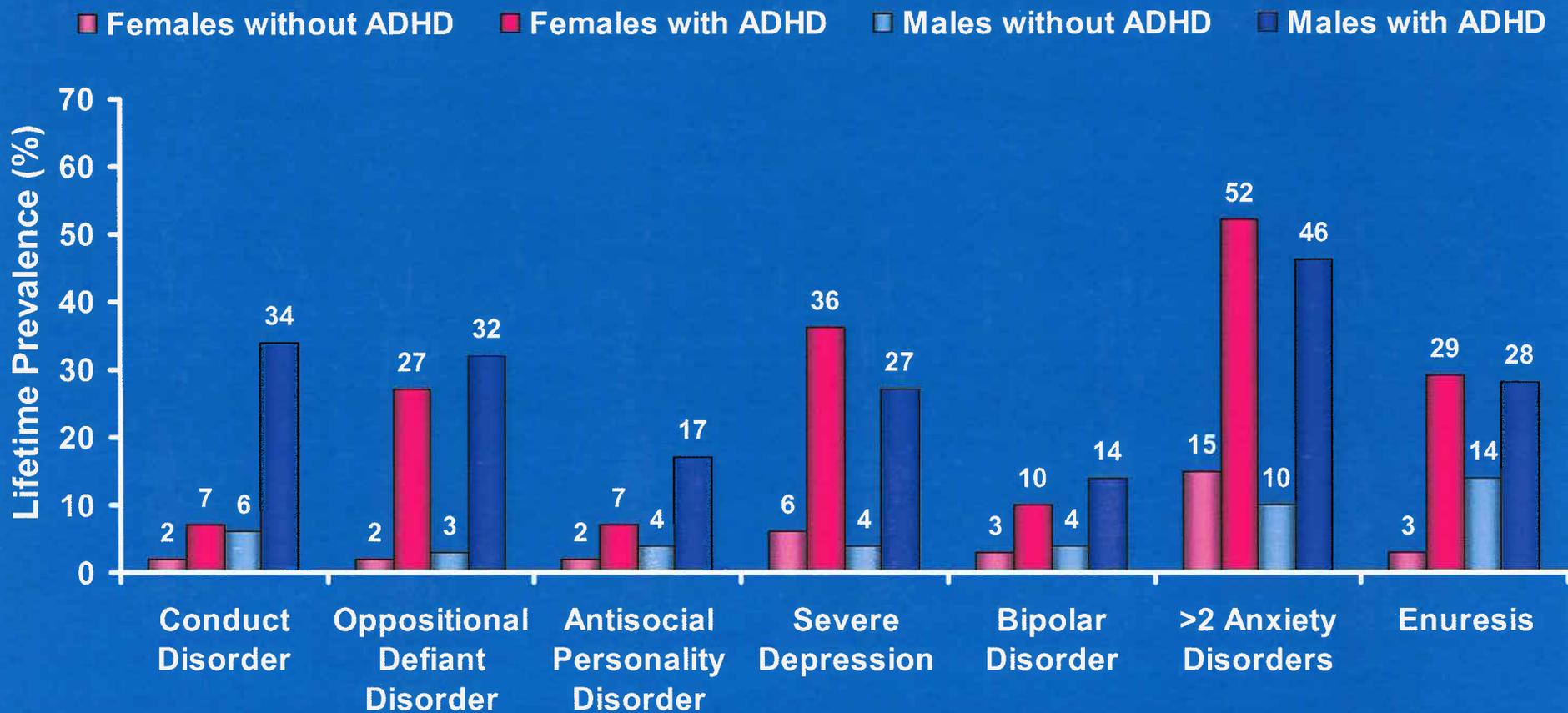
Impaired Family and Peer Relationships

Motor vehicle accidents

Occupational/vocational difficulties

American Academy of Pediatrics. *Pediatrics*. 2000;105:1158-1170.
Kelly PC et al. *Pediatrics*. 1989;83:211-217.
Murphy K et al. *Compr Psychiatry*. 1996;37:393-401.
Biederman J. *J Clin Psychiatry*. 2004;65:3-7.
Barkley RA et al. *Pediatrics*. 1996;98:1089-1095.
Swensen A et al. *J Adolesc Health*. 2004;35:346.e1-9.

Associated Comorbidities Add to Personal and Economic Costs of ADHD in Adults *[Biederman 2004, p. 5 B]*



Biederman J. *J Clin Psychiatry*. 2004;65(suppl 3):3-7.

Desired Treatment Outcomes in Adult ADHD

- Work function [*Weiss et al. 2004, p.32B, C*]
 - Improved time management, organizational skill and productivity
 - Meeting deadlines
 - Maintaining attention during meetings
- Home/personal function [*Weiss et al. 2004, p.32B, C*]
 - Better family interactions
 - Parenting, helping children with homework, spousal interactions
 - Improved time management and organizational skills
 - Able to pay bills, not losing sight of necessary activities/deadlines, planning activities
 - Able to control impulses
 - Avoiding speeding/recklessness during driving
 - Decreased substance use

Nonpharmacological Interventions

- Psychoeducation for patient and family members
 - Support groups (www.chadd.org) [*www.chadd.org, p1A*]
 - Coaching (www.coaching.com) [*www.coaching.com, p1A*]
 - Psychotherapy
 - Cognitive behavioral therapy may be useful¹ [*Safren et al. 2005, 837A*]

1. Safren A et al. *Behaviour Research and Therapy*. 2005;43:831-842.

FDA-Approved Medications Indicated for ADHD in Adults*

[Weiss et al. 2004, p.34 A,B,C]

Stimulants	Brand Names	Approval Date (US)
d-methylphenidate	Focalin [®] XR	May, 2005
Mixed amphetamine salts	Adderall XR [®]	August, 2004
Nonstimulant		
Atomoxetine	Strattera [®]	November, 2002

- Focalin XR is the only methylphenidate formulation approved in adults

*As of May 2006.

Adderall XR[®] is a trademark of Shire US Inc.; Strattera[®] is a trademark of Eli Lilly and Co.



Focalin[®] XR: A Single-Isomer Formulation of Methylphenidate

- Therapeutic effect of racemic *d,l*-MPH resides primarily in the *d*-enantiomer¹ [*Srinivas et al 2001, p.1207A*]
- Focalin XR contains only the pharmacologically active *d*-enantiomer of *d,l*-MPH² [*Focalin XR PI 2006, p.1A*]
 - Only need half the dose of racemic MPH [*Focalin XR PI 2006 p.22A, 2C; Markowitz 2005 Abstract A*]
- Advantages of single-isomer therapeutics may include³: [*Hutt 2003,p.7A,8A*]
 - More selective pharmacologic profile
 - Potential for improved therapeutic index
 - Less complex pharmacokinetic profile
 - Potential for decreased drug interactions

1. Srinivas NR et al. *J Pharm Sci.* 2001;90:1205-1215. 2. Focalin XR [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; June 2006. 3. Hutt AJ et al. *Acta Facult Pharm Univ Comeniana.* 2003;50:7-23.



Focalin[®] XR: A Once-Daily Formulation of *d*-MPH

- Rapid onset, similar to immediate-release Focalin [*Focalin XR PI 2006, p.1A, 2B*]
- Uses SODAS[®] extended-release technology to mimic BID dosing [*Focalin XR PI 2006, p.2A*]
 - 50% of dose released immediately upon administration
 - 50% of dose released ≈4 h later for extended duration of action
- Once-daily dose in morning eliminates need for midday dose [*Focalin XR PI 2006, p.21A*]
- Flexible, individualized dosing [*Focalin XR PI 2006, p.1B*]
- Smooth response curve over postdose interval [*Focalin XR PI 2006, p. 2C, 4A*]

	<i>d</i> -MPH		
Dose	5 mg	10 mg	20 mg
Immediate release	50%		
	2.5 mg	5 mg	10 mg
Second release	50%		
	2.5 mg	5 mg	10 mg

Focalin XR [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; June 2006.



Focalin[®] XR
(dexmethylphenidate HCl)
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Efficacy and Safety in the Adult Population

Focalin[®] XR in Adults With ADHD: 5-Week Study

- Objective: to evaluate the efficacy and safety of Focalin XR administered once daily as compared with placebo in adults meeting DSM-IV criteria for ADHD [*Spencer 2006 p. 5B*]
- 5-week, randomized, multicenter, double-blind, fixed-dose, parallel-group design [*Spencer 2006 p. 5A, 6A*]
 - Focalin XR 20 mg/day (n=58)
 - Focalin XR 30 mg/day (n=55)
 - Focalin XR 40 mg/day (n=55)
 - Placebo (n=53)
- Symptoms were assessed for the previous week [*CSR 2302, p.25A*]

Focalin XR 20 mg is currently the maximum dose approved in adults.
Study 2302.

Spencer T et al. *Biol Psychiatry*. 2006. In press.



Focalin[®] XR in Adults With ADHD: Outcome Variables

- Primary:
 - Change from baseline in DSM-IV ADHD RS Total [*CSR 2302, 11A*][*Spencer 2006 p. 6C*]
- Secondary: [*Spencer 2006 p. 6-7D*]
 - Change from baseline in DSM-IV ADHD inattention and hyperactivity/impulsivity subscales
 - Change from baseline in CAARS Self-Report and Observer Scores
 - Proportion of patients with improvement of $\geq 30\%$ in ADHD Rating Scale Total
 - Proportion of patients with improvement on CGI-I

Study 2302.

Spencer T et al. *Biol Psychiatry*. 2006. In press.



Focalin® XR in Adults With ADHD: Demographic and Baseline Characteristics *[Spencer 2006 p. 9B, 25A]*

Variable	Placebo (n=53)	Focalin XR 20 mg (n=58)	Focalin XR 30 mg (n=55)	Focalin XR 40 mg (n=55)
Gender				
Male (%)	50.9	55.2	61.8	61.8
Mean age (y)	38.1	39.1	39.1	38.2
Race (%)				
Caucasian	75.5	100	87.3	78.2
Black	5.7	0	5.5	7.3
Asian	5.7	0	0	7.3
Other	13.2	0	7.3	7.3
ADHD Subtype (%)				
Inattentive	22.6	29.3	25.5	29.1
Hyperactive/Impulsive	1.9	3.4	5.5	1.8
Combined	75.5	67.2	69.1	69.1
Duration of ADHD (y)	31.1	32.9	33.5	31.9
Past ADHD Medication (% yes)	49.1	34.5	21.8	40.0
Baseline ADHD-RS total	37.5	36.9	36.9	36.7

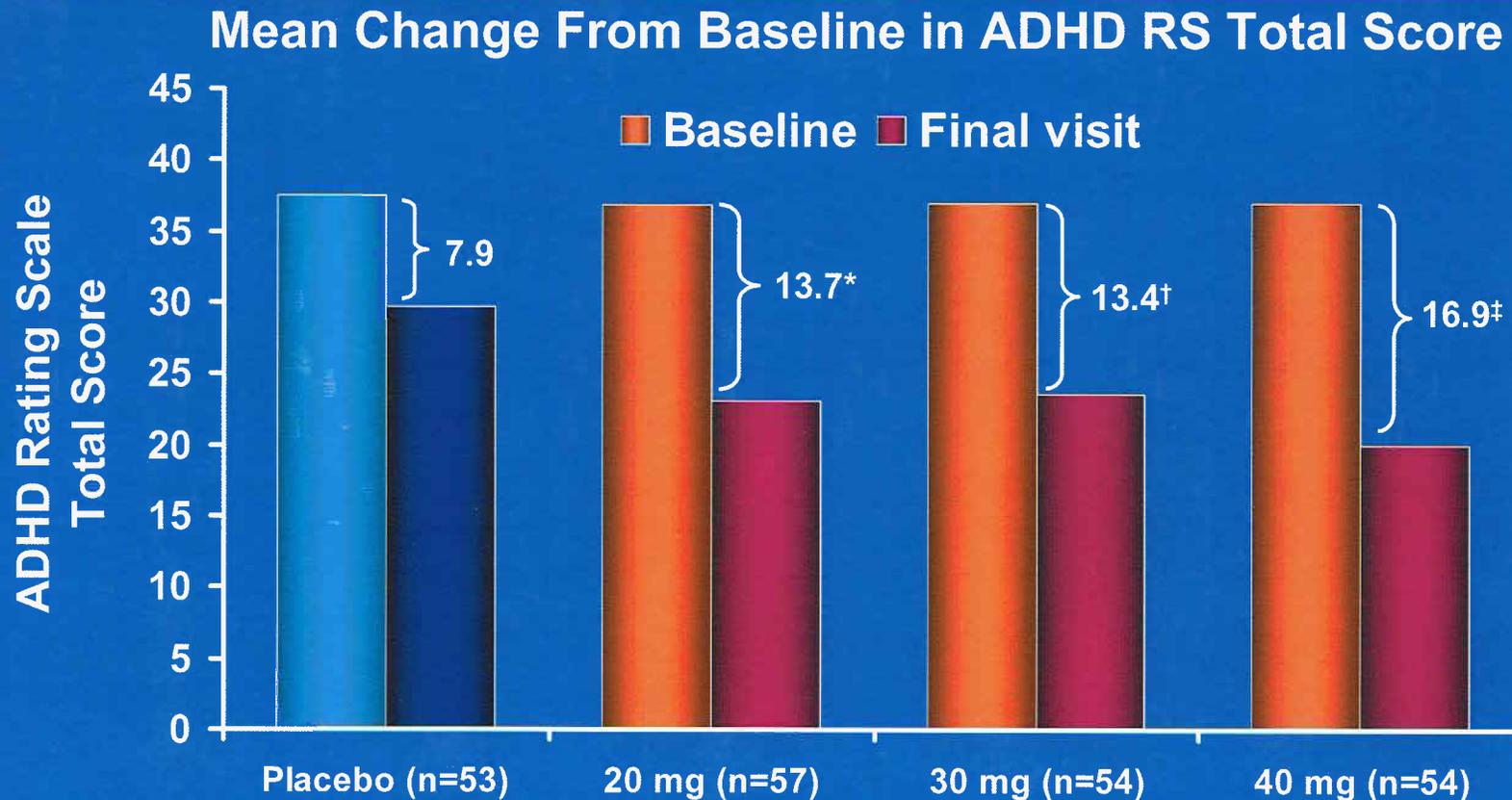
Study 2302.

Spencer T et al. *Biol Psychiatry*. 2006. In press.



Focalin[®] XR Significantly Reduced ADHD Total Symptom Scores

[Spencer 2006 p. 10B]



Focalin XR 20 mg is currently the maximum dose approved in adults.

* $P < 0.01$, † $P < 0.05$, ‡ $P = 0.001$ vs placebo.

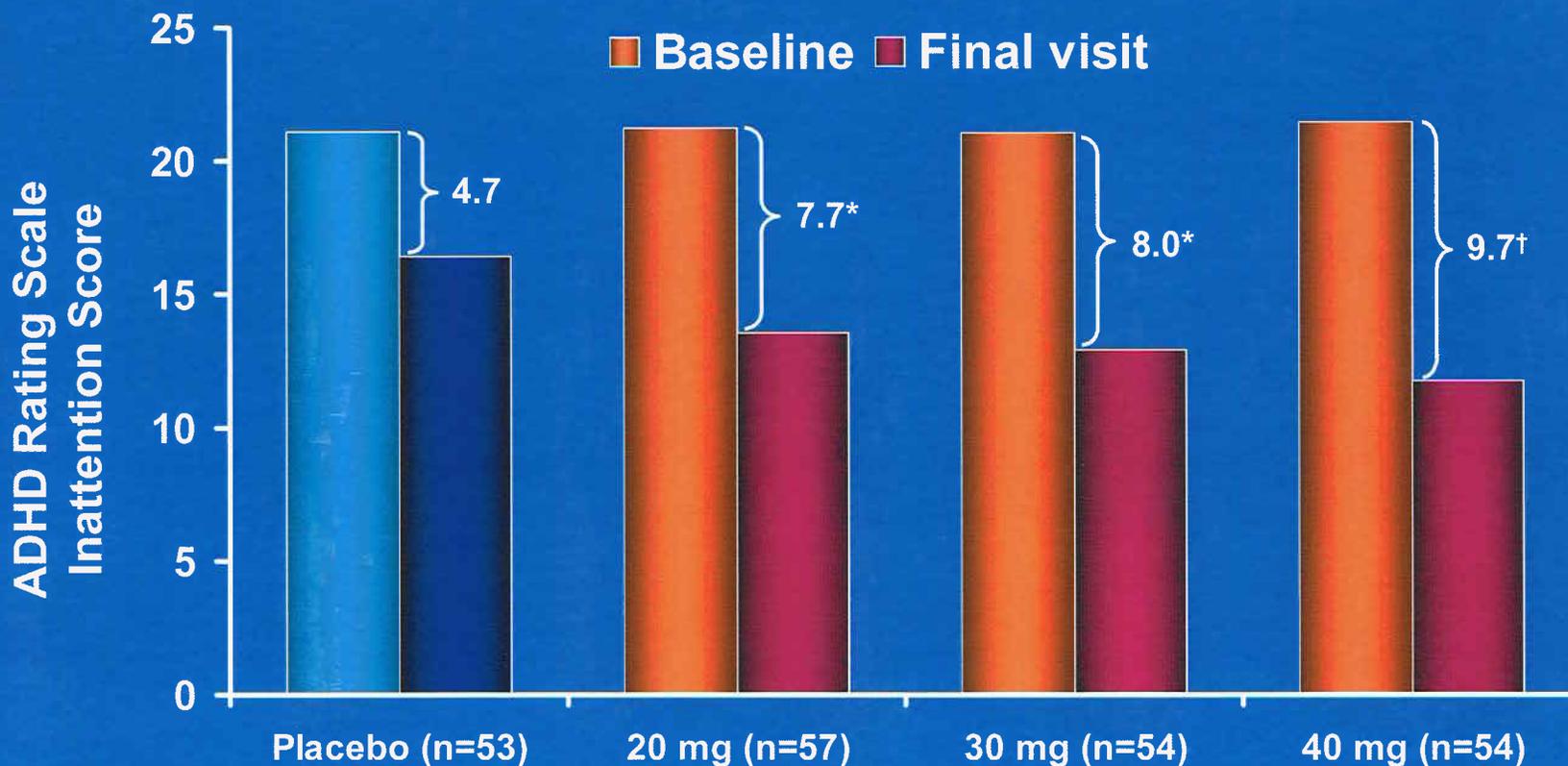
Study 2302.

Spencer T et al. *Biol Psychiatry*. 2006. In press.



Focalin[®] XR Significantly Reduced Inattentive Symptoms [CSR 2302, p47A]

Mean Change From Baseline in ADHD RS Inattention Subscale



Focalin XR 20 mg is currently the maximum dose approved in adults.

* $P < 0.05$, † $P < 0.001$ vs placebo.

Study 2302.

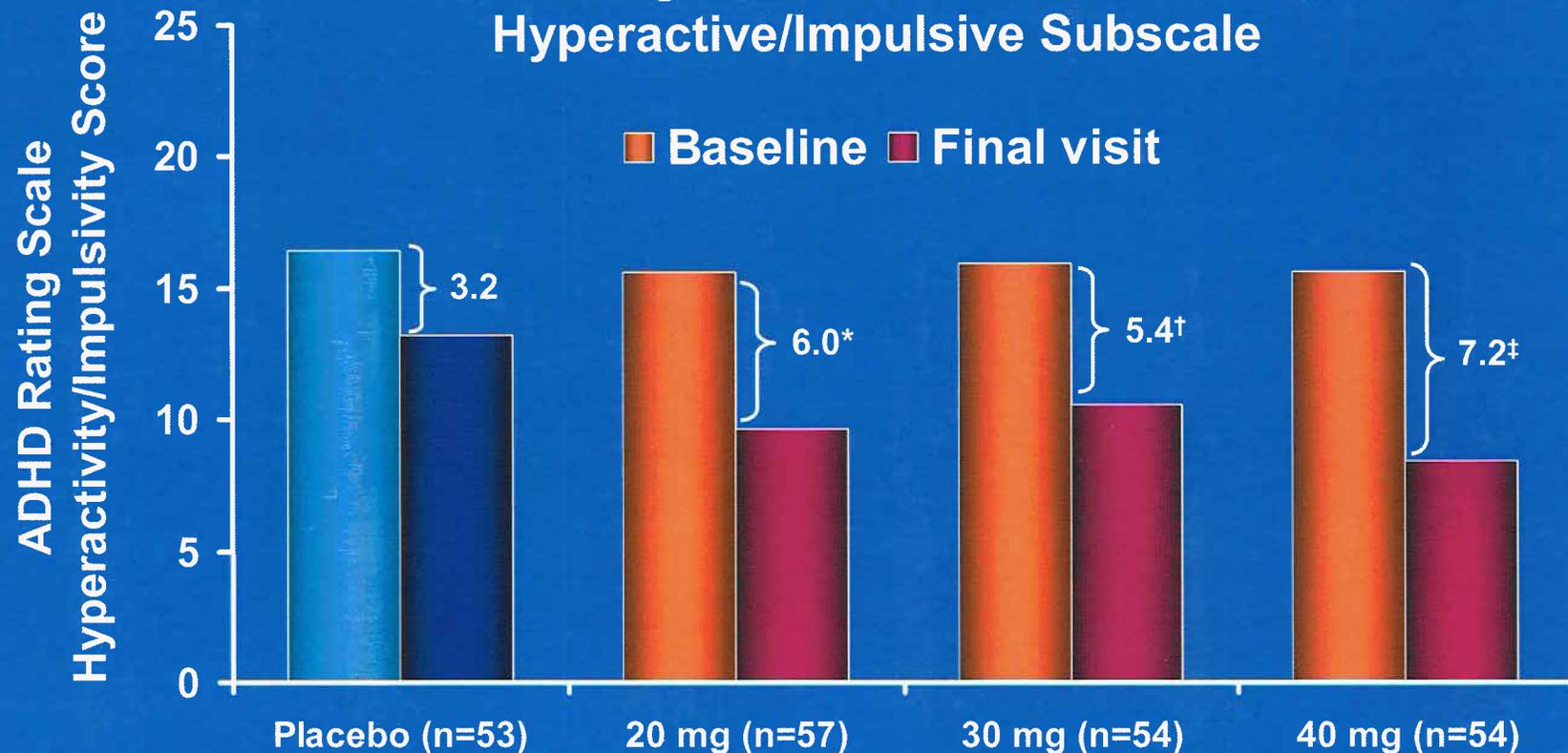
Data on file, Novartis Pharmaceuticals Corporation.



Focalin[®] XR Significantly Reduced Hyperactivity/Impulsivity

[CSR 2302, p47B]

Mean Change From Baseline in ADHD RS Hyperactive/Impulsive Subscale



Focalin XR 20 mg is currently the maximum dose approved in adults.

* $P < 0.01$, † $P < 0.05$, ‡ $P < 0.001$ vs placebo.

Study 2302.

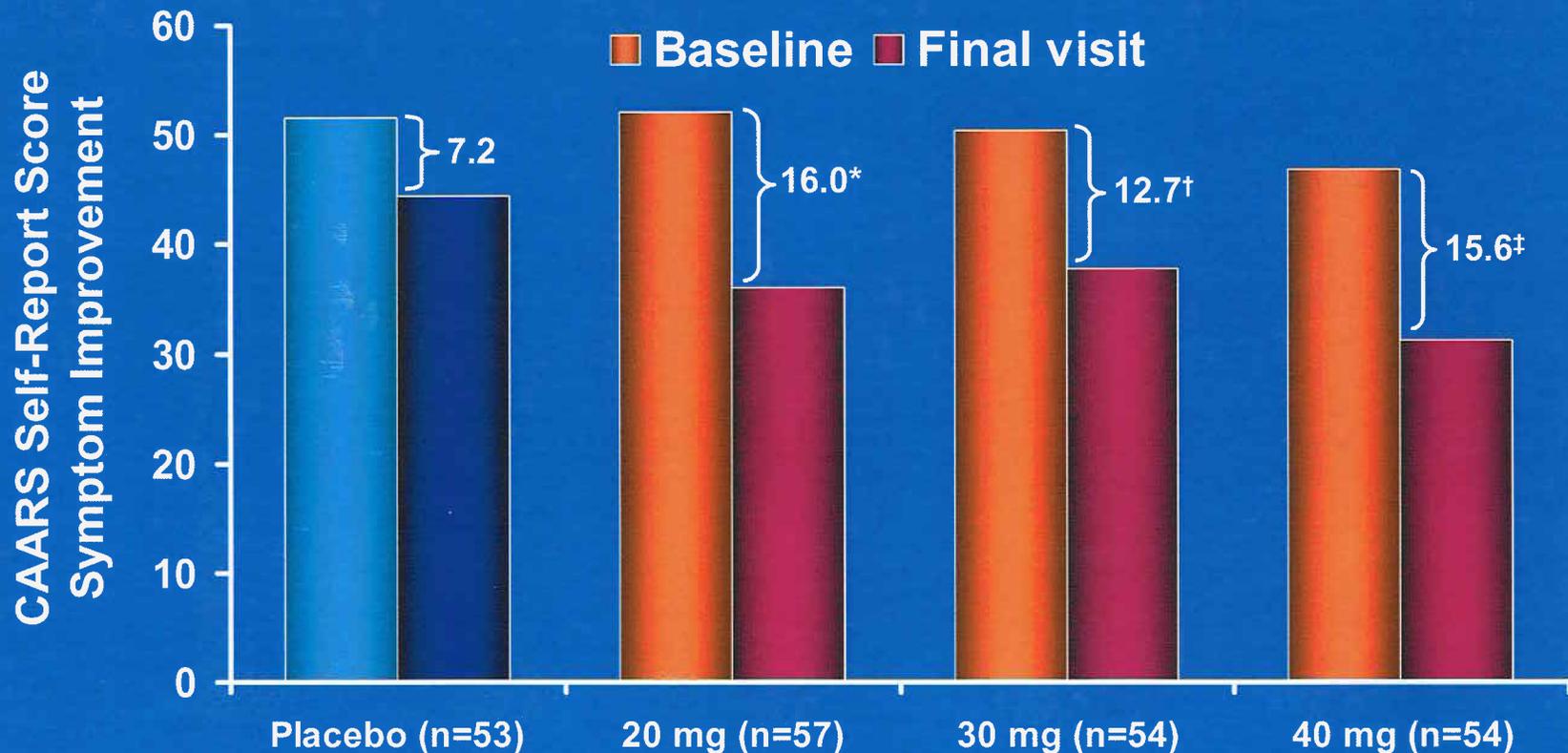
Data on file, Novartis Pharmaceuticals Corporation.



Patients Noted Significant Improvement in ADHD Symptoms

[Spencer 2006 p. 12A]

Mean Change From Baseline in CAARS Self-Report Scale



Focalin® XR 20 mg is currently the maximum dose approved in adults.

*P=0.003, †P=0.045, ‡P=0.001 vs placebo.

Study 2302.

Spencer T et al. *Biol Psychiatry*. 2006. In press.



Focalin[®] XR in Adults With ADHD: Other Secondary Outcomes

- Significantly improved outcomes were achieved with Focalin XR versus placebo
 - Greater improvement in CAARS observer reports [*Spencer 2006 p. 12A*]
 - More patients experienced a 30% or greater improvement in ADHD-RS [*Spencer 2006 p. 11A*]
 - Significantly greater number of “responders” on the CGI-I [*Spencer 2006 p. 11B, 11C*]
- Focalin XR patients perceived a rapid onset of action and all day coverage with one dose [*CSR 2302, p.52B, 53A*]

Study 2302.

Spencer T et al. *Biol Psychiatry*. 2006. In press.
Data on file, Novartis Pharmaceuticals Corporation.



6-Month Open-Label Extension of Treatment in Adults With ADHD

- Subjects who completed the 5-week double-blind study were eligible to continue into a 6-month, open-label, flexible dose extension *[Adler et al. 2005, p.1D]*
- Initial dose of 10 mg/day with individualized titration to a maintenance dose of between 20 mg and 40 mg/day *[Adler et al. 2005, p.1D]*
- *Primary outcome:* change in ADHD-RS from final double-blind visit (week 5) to final open-label visit *[Adler et al. 2005, p.1E]*
- *Secondary outcome:* proportion of patients who improved on CGI-I from baseline to final open-label visit *[Adler et al. 2005, p.1F]*

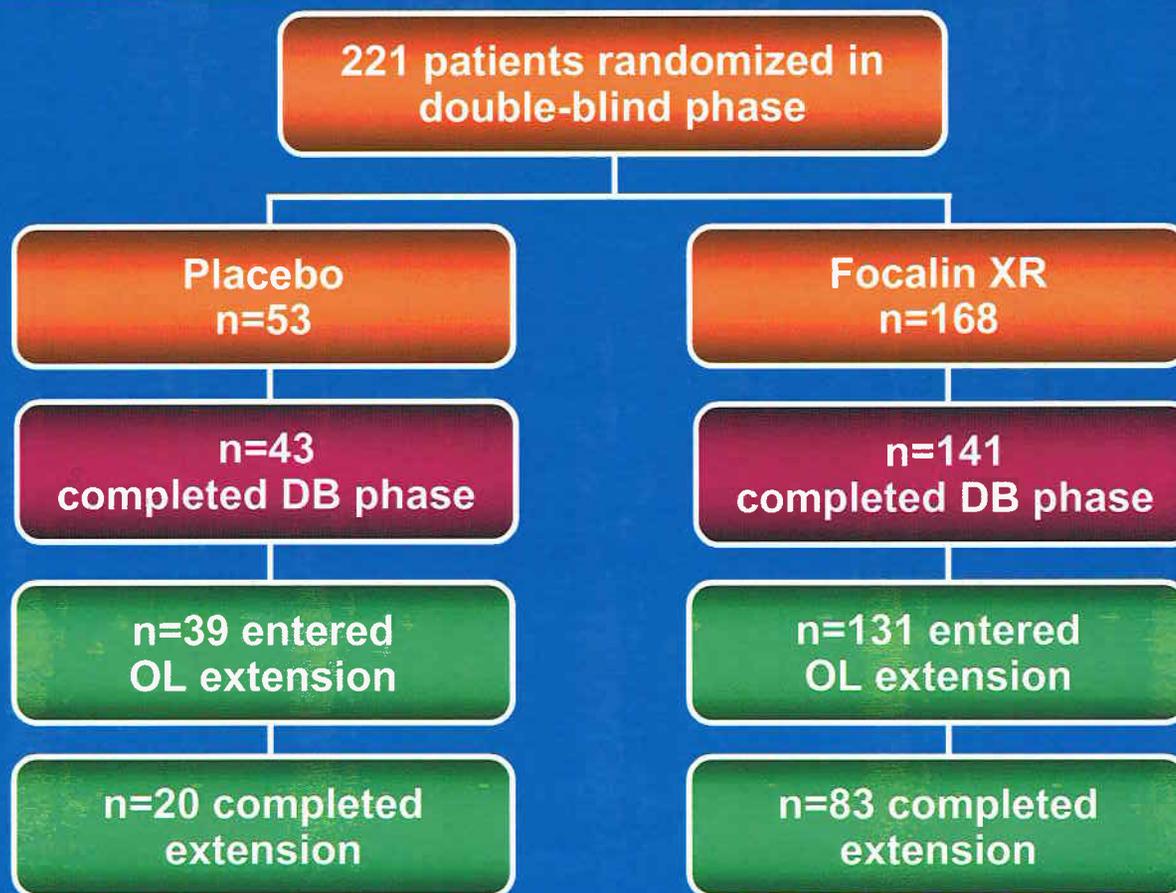
Study 2302E1.

Adler LA et al. Poster. APA; 2005; Atlanta, Ga.



Focalin[®] XR in Adults With ADHD: Patient Flow in Double-Blind and Open-Label Studies

[Adler et al. 2005, p.1G; CSR 2302E1, p.25A, 26A,B]



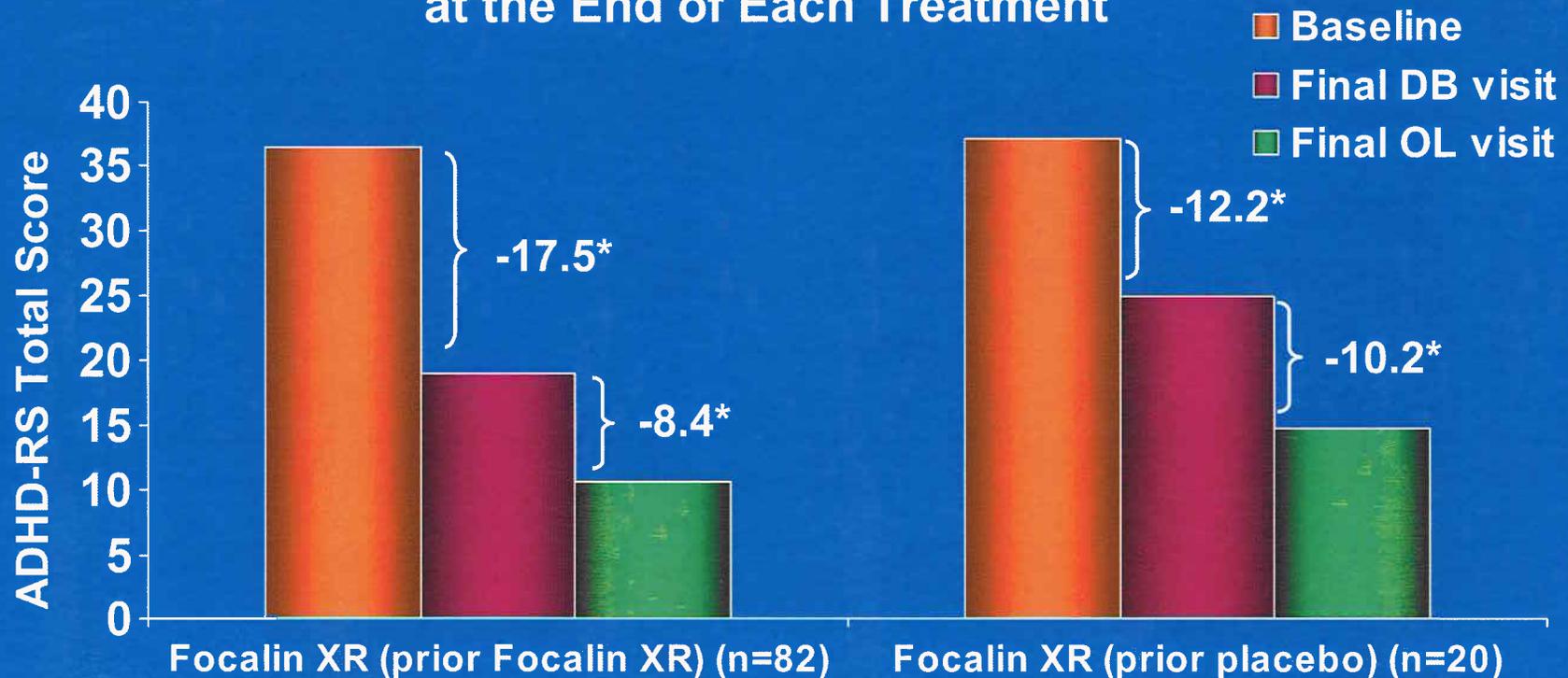
Study 2302E1.

Data on file, Novartis Pharmaceuticals Corporation.



Focalin[®] XR Demonstrated Long-Term Symptom Control As Shown by ADHD Total Symptom Scores [Adler 2005 L]

Change in ADHD-RS Total Score at the End of Each Treatment



Dose range of Focalin XR in open-label study was between 10 and 40 mg/day.
Mean exposure to study drug was 4.5 months.

* $P < 0.001$ vs baseline.
Studies 2302 and 2302E1.

Adler LA et al. Poster. APA; 2005; Atlanta, Ga.

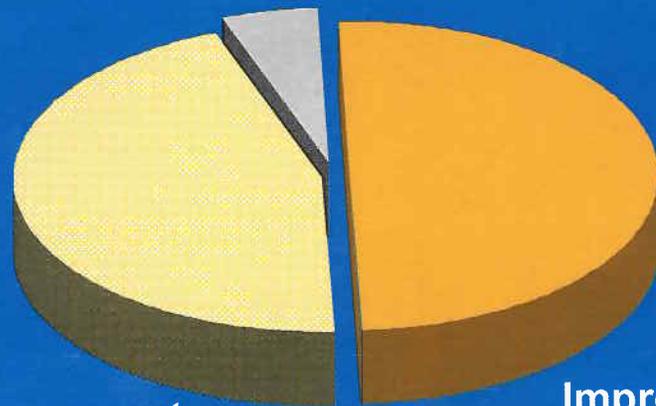


Patients Continued to Experience Symptom Improvement With Focalin[®] XR

[CSR 2302E1, post-text table 9.2-4, p.36B; Adler 2005 K]

Focalin XR (Prior Placebo)
(n=20)

No Improvement
5.0%

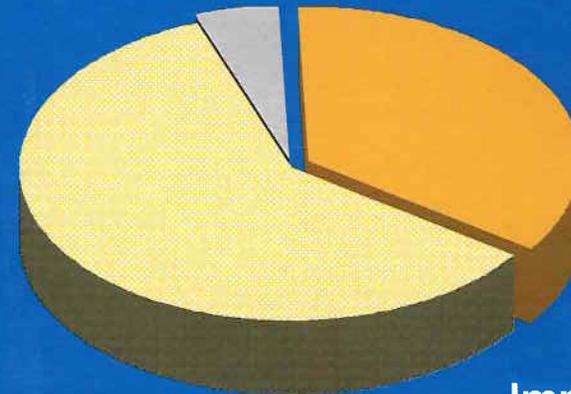


Improvement
in DB phase
45.0%

Improvement
in OL phase
95.0%

Focalin XR (Prior Focalin XR)
(n=82)

No Improvement
4.9%



Improvement
in DB phase
59.8%

Improvement
in OL phase
95.1%

*Improvement = score of 1: "very much improved" or 2: "much improved."
DB = double-blind; OL = open-label.
Studies 2302 and 2302E1.

Data on file, Novartis Pharmaceuticals Corporation.
Adler LA et al. Poster. APA; 2005; Atlanta, Ga.



Focalin[®] XR in Adults With ADHD: Summary of Efficacy Results

- Focalin XR is effective in treating adult ADHD [*Adler et al. 2005, 1*] [*Spencer et al 2004E*]
- Improvements are recognized by patients and blinded observers (family, clinicians) [*CSR 2302, p.49A, 50A, 51A, 52A*]
- Improvements are observed in multiple settings (home, work, clinic, laboratory) [*CSR 2302, p.26AB*]
- Improvements are sustained over 6 months [*Adler et al. 2005, p.1B, 1C*]
- Patients perceived a rapid onset of action and all day coverage with one dose [*CSR 2302, p.52B*][*CSR 2302, p.53A*]

Studies 2302 and 2302E1.



Most Frequent Adverse Events Were As Expected for Stimulants

[CSR 2302, p.55A,B, 56C]

Number (%) of Patients Experiencing AEs at Frequencies $\geq 10\%$
in the 5-week double-blind study

	Placebo n=53	Focalin [®] XR 20 mg n=57	Focalin XR 30 mg n=54	Focalin XR 40 mg n=54
N(%) patients with AEs				
Headache	10 (18.9)	15 (26.3)	16 (29.6)	21 (38.9)*
Decreased appetite	6 (11.3)	11 (19.3)	9 (16.7)	10 (18.5)
Insomnia	6 (11.3)	10 (17.5)	7 (13.0)	10 (18.5)
Dry Mouth	2 (3.8)	4 (7.0)	11 (20.4)*	11 (20.4)*
Nausea	2 (3.8)	6 (10.5)	1 (1.9)	3 (5.6)
Feeling jittery	1 (1.9)	5 (8.8)	10 (18.5)*	5 (9.3)
Anxiety	1 (1.9)	3 (5.3)	6 (11.1)	6 (11.1)

Focalin XR 20 mg is currently the maximum dose approved in adults.

* $P < 0.05$ vs placebo using a chi-square test.

Study 2302.

Data on file, Novartis Pharmaceuticals Corporation.



Most Frequent Adverse Events (≥10% Overall) Over 6 Months [Adler et al. 2005 A, J]

Summary of Adverse Events in 6-Month Open-Label Extension

	Mean Daily Dose of Focalin® XR			
	≤20 mg/day n=41	20-30 mg/day n=64	>30 mg/day n=65	All N=170
N(%) patients with AEs				
Headache	8 (19.5)	24 (37.5)	15 (23.1)	47 (27.6)
Insomnia	10 (24.4)	21 (32.8)	3 (4.6)	34 (20.0)
Decreased appetite	4 (9.8)	16 (25.0)	10 (15.4)	30 (17.6)
Feeling Jittery	12 (29.3)	6 (9.4)	5 (7.7)	23 (13.5)
URI	1 (2.4)	10 (15.6)	11 (16.9)	22 (12.9)
Anxiety	5 (12.2)	9 (14.1)	7 (10.8)	21 (12.4)
Dry Mouth	2 (4.9)	8 (12.5)	11 (16.9)	21 (12.4)

Focalin XR 20 mg is currently the maximum dose approved in adults.
Study 2302E1.

Adler LA et al. Presented at the 158th Meeting of the American
Psychiatric Association, May 21-25, 2005.



No Clinically Significant Changes in Vital Signs or Body Weight Vs Placebo

[CSR 2302E pg. 62A,C; Spencer 2006 p. 13A, 14A,B]

Mean Change From Baseline in Vital Signs and Weight

Variable	5-Week Double-blind Study		6-Month Extension
	Focalin [®] XR (all doses) n=168	Placebo n=53	Focalin XR 10-40 mg/d N=170
Systolic BP (mmHg)	-0.5 ± 11.5	-1.7 ± 11.3	2.3 ± 12.6
Diastolic BP (mmHg)	1.0 ± 8.4	0.3 ± 7.8	1.6 ± 9.8
Pulse	4.4 ± 11.0*	-1.4 ± 9.3	3.7 ± 11.3
Weight (kg)	-1.4 ± 2.1*	-0.1 ± 3.9	-1.8 ± 6.8

- No patients receiving Focalin XR experienced clinically notable changes in vital signs, although clinically notable weight loss occurred in 19.4% of treated patients over 6 months

Focalin XR 20 mg is currently the maximum dose approved in adults.

*P<0.05 vs placebo using a t-test.

Studies 2302 and 2302E1.

Spencer T et al. Presented at the 157th Meeting of the American Psychiatric Association, May 1-6, 2004.

Data on file, Novartis Pharmaceuticals Corporation.



Focalin[®] XR in Adults With ADHD: Summary of Safety

- The most frequent AEs associated with short-term and longer-term treatment were transient, mild to moderate, and consistent with those seen in stimulants *[CSR 2302E1 p. 46A]*
- Minimal changes in vital signs over 6 months *[CSR 2302E1 p. 53A]*
- Some weight loss over 6 months *[CSR 2302E1 p. 53A]*

Study 2302E1.
Data on file, Novartis Pharmaceuticals Corporation.



Focalin[®] XR: Indications

- Focalin XR (dexamethylphenidate hydrochloride) extended-release capsules is indicated for the treatment of Attention deficit Hyperactivity Disorder (ADHD) in patients aged 6 years or older [*Focalin XR PI pg 8A*]
- Focalin XR is indicated as an integral part of a total treatment program for ADHD that may include other measures (psychological, educational, social) for patients with this syndrome [*Focalin XR PI pg 8B*]

Focalin[®] XR: Contraindications

- **Agitation**
 - Focalin XR (dexmethylphenidate hydrochloride) extended-release capsules is contraindicated in patients with marked anxiety, tension, and agitation, since the drug may aggravate these symptoms. *[Focalin XR PI 2006 p.9A]*
- **Hypersensitivity to methylphenidate**
 - Focalin XR is contraindicated in any patient known to be hypersensitive to methylphenidate, or any components of this product. *[Focalin XR PI 2006 p.9B]*

These contraindications are class labeling and are not specific to Focalin XR. *[Biederman 2003, p. 9C]*

Focalin XR [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; June 2006.



Focalin[®] XR: Contraindications (cont)

- **Glaucoma**
 - Focalin XR is contraindicated in patients with Glaucoma [*Focalin XR PI 2006 p.9C*]
- **Tics**
 - Focalin XR is contraindicated in patients with motor tics or with a family history or diagnosis of Tourette's syndrome [*Focalin XR PI 2006 p.9C*]
- **Monoamine Oxidase Inhibitors**
 - Focalin XR is contraindicated during treatment with monoamine oxidase inhibitors, and also within a minimum of 14 days following discontinuation of treatment with a monoamine oxidase inhibitor (hypertensive crisis may result) [*Focalin XR PI 2006 p.9D*]

These contraindications are class labeling and are not specific to Focalin XR. [*Biederman 2003, p. 9B*]

Focalin XR [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; June 2006.



Warnings – 1 of 2

- Stimulants should generally not be used in children, adolescents, or adults with known serious structural cardiac abnormalities, cardiomyopathy, serious heart rhythm abnormalities, or other serious cardiac problems. Use with caution in treating patients with underlying medical conditions that might be compromised by increases in blood pressure or heart rate such as those with pre-existing hypertension, heart failure, recent myocardial infarction, or ventricular arrhythmia. Before initiating treatment, patients should have careful history and physical exam to assess for presence of cardiac disease. *[Focalin XR PI 2006 p.10AB)*

These warnings were required by the FDA for all CNS stimulant products to treat ADHD in May 2006.

Focalin XR [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; June 2006.

Warnings – 2 of 2

- Use with caution in psychosis or bipolar disorder. Discontinuation of treatment may be appropriate in the presence of treatment-emergent psychotic or manic symptoms. While aggressive behavior is often observed in children or adolescents with ADHD, patients beginning treatment should be monitored for the appearance of or worsening of aggressive behavior or hostility. [*Focalin XR PX 2006 p.11AB*]
- Suppression of growth has been reported with long-term use of stimulants. Stimulants should be used with caution in patients with a prior history of seizures or EEG abnormalities. Difficulties with accommodation and blurring of vision have been reported with stimulant treatment. (See WARNINGS.) [*Focalin XR PI 2006 p.11C, 12ABC*]

These warnings were required by the FDA for all CNS stimulant products to treat ADHD in May 2006.

Focalin XR [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; June 2006.

Special Safety Issues: Controlled Substance Class

- Focalin[®] XR is a Schedule II controlled substance [*Focalin XR PI 2006 p.20A*]
- Should be given cautiously to patients with history of drug dependence or alcoholism [*Focalin XR PI 2006 p.12D*]
- Chronic abuse can lead to marked tolerance and psychological dependence [*Focalin XR PI 2006 p.12D*]
- Frank psychotic episodes can occur, especially with parenteral abuse [*Focalin XR PI 2006 p.12D*]
- Withdrawal from abuse must be carefully supervised to monitor for severe depression [*Focalin XR PI 2006 p.12D*]
- Withdrawal after chronic therapeutic use may unmask symptoms of underlying disorder that may require follow-up [*Focalin XR PI 2006 p.12D*]

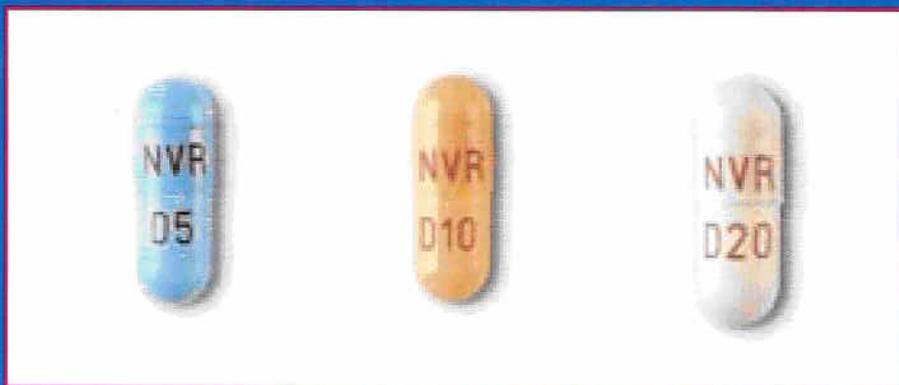
These safety issues are class labeling and are not specific to Focalin XR. [*Greenhill 2002; p.28SA, 36SAB*]

Focalin XR [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; June 2006.



Focalin[®] XR: Dosing Flexibility

- Capsule strengths: 5 mg, 10 mg, and 20 mg [*Focalin XR PI 2006 p. 1B*]
- Can administer by sprinkling capsule contents on applesauce [*Focalin XR PI 2006 p. 21B*]



Focalin XR [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; June 2006.



Dosage and Administration

Recommended Dosing Guidelines

Treatment-naïve patients <i>[Focalin XR 2006 PI p. 21D,E]</i>	Pediatric:	5 mg/day Dosage may be adjusted in 5-mg/week intervals to a maximum of 20 mg/day for pediatric patients
	Adult:	10 mg/day Dosage may be adjusted in 10-mg/week intervals to a maximum of 20 mg/day for adults
Patients currently receiving racemic <i>d,l</i>-MPH <i>[Focalin XR PI 2006 pg. 22A]</i> <ul style="list-style-type: none">Includes Ritalin[®] LA, Concerta[®], and Metadate[®] CD	Pediatric or adult:	Half the currently-prescribed daily dose of racemic <i>d,l</i> -MPH

Focalin XR [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; June 2006.



Focalin[®] XR: Dose Reduction and Discontinuation

- Focalin XR dose should be reduced or drug discontinued if paradoxical aggravation of symptoms or other AEs occur [*Focalin XR PI 2006 p. 22B*]
- If symptomatic improvement is not observed after appropriate dosage adjustment over 1 month, drug should be discontinued [*Focalin XR PI 2006 p. 22C*]

This is class labeling and is not specific to Focalin XR.
Focalin XR [package insert]. East Hanover, NJ: Novartis
Pharmaceuticals Corporation; June 2006.



Maintenance/Extended Treatment

- No evidence from controlled trials to indicate how long patients with ADHD should be treated with Focalin[®] XR [*Focalin XR PI 2006 p. 22D*]
- Pharmacological treatment may be needed for extended periods [*Focalin XR PI 2006 p. 22D*]
- Effectiveness of Focalin XR for long-term use (>7 weeks) has not been systematically evaluated in controlled trials [*Focalin XR PI 2006 p. 22D, 7A,B*]
- Patients should periodically be re-evaluated, with periods off medication [*Focalin XR PI 2006 p. 22D*]
- Improvement may be sustained when the drug is temporarily or permanently discontinued [*Focalin XR PI 2006 p. 22D*]

Summary of Focalin® XR in Adults With ADHD

[summary slide; supported by previous slides]

- Focalin XR provides improvements in core symptoms of ADHD in adults with a single daily dose
 - Improvement in attention
 - Improvement in hyperactivity/impulsivity
 - Symptom improvement across multiple domains may reduce distractibility, enhance productivity, and improve social and family interactions
 - Rapid onset and all-day duration
- Focalin XR is safe and tolerable in adults



Case Study: NB

New Patient with Adult ADHD

Clinical Case Study: NB

Patient: NB

Visit Date: 2/8/06

CC: R/O ADHD

HPI: 36 y/o C ♂. Employed as an insurance broker. Presenting with occupational and personal distress. Reports difficulty in the office, feels unproductive despite working >60 hrs/wk. Difficulty sitting through meetings, restlessness, frustration, interrupts others, makes inappropriate comments.

Social Hx: Hx of risk-taking behavior, poor driving record (2 speeding tickets in past month, MVA 1999), 3 jobs in 5 years. Divorced, no children. "Bad temper". Unremarkable school performance as a child (below average grades, some behavioral/disciplinary issues).

Clinical Case Study: NB

Family Hx: Parents living and healthy. Divorced. 1 sister, healthy, second marriage, 3 children.

PMH: Pt denies any past medical problems

Medications: Pt denies taking any medications

Allergies: NKDA

PE: VS: BP 118/77, pulse 74, wt 185 lbs height 5'10"

GEN: otherwise healthy appearing patient

HEENT: atraumatic/normocephalic, PERRL, EOMI, supple neck, no thyromegaly

Cardiovascular: regular heart rate and rhythm, w/o murmurs

Impression: ADHD hyperactive/impulsive subtype

Treatment Plan: Begin patient on ADHD medication – QD Focalin® XR
10 mg/day to be titrated to 20 mg/day

Clinical Case Study: NB

Discussion

- Hyperactivity in adults is different than in children
 - Less obviously hyperactive
 - Talking excessively, “workaholic” but not effective, impatient, impulsive, traffic accidents/speeding, easily frustrated
- ADHD medications indicated for adults include Strattera[®], Adderall XR[®], and Focalin[®] XR
 - Stimulant medications to treat ADHD are safe, effective, and well-studied
 - Focalin XR was chosen as first-line treatment because it offers rapid onset and all-day duration of coverage with once-daily dosing and has a good tolerability profile

Case Study: AV

New Patient with Adult ADHD

Clinical Case Study: AV

Patient: AV

Visit Date: 1/13/06

CC: Referral to R/O ADHD

HPI: 28 y/o C ♀. Works for a telephone company, married, 2 children.

Son has ADHD, his pediatrician referred AV to R/O ADHD.

Forgetful, has a low frustration tolerance, argues with family a lot.

Has difficulty being productive at work (procrastinates, does not finish tasks, disorganized). Has low self-esteem.

AV has found that she needs to stick to a schedule in order to get things done, but does not do well if plans change, family complains that she is inflexible. Unable to coordinate work and parenting/spouse demands. She is very concerned that her behavior is affecting her family.

Clinical Case Study: AV

Social Hx: Smoker 1 pack/day. Social drinker. Lives with husband and 2 children. She received average grades when in school, used to “daydream” or “doodle” and miss or forget things. Never had many friends, but had a few close ones

Family Hx: Both parents living, 2 children, son w/ ADHD, otherwise healthy

PMH: Broken shoulder @ age 9, sprained wrist @ age 14.

Medications: Pt denies taking any medications

Allergies: NKDA

PE: VS: BP 111/72, pulse 70, wt 135 lbs height 5'4"

GEN: otherwise healthy appearing patient

HEENT: atraumatic/normocephalic, PERRL, EOMI, supple neck, no thyromegaly

Cardiovascular: regular heart rate and rhythm, w/o murmurs

Impression: ADHD inattentive subtype

Treatment Plan: Begin patient on ADHD medication – QD Focalin® XR
10 mg/day to be titrated to 20 mg/day

Clinical Case Study: AV Discussion

- Inattentive symptoms in adults may include:
 - Forgetfulness, losing things, organizational problems, overreacting to frustration, procrastination
 - Inattentive subtype often missed in children
- Focalin XR has demonstrated improvements in the core symptoms of ADHD (including attention) with a single daily dose
 - Rapid onset and all-day duration
- ADHD treatment may help AV with her disorganization and frustration, which may help improve her social and family interactions

▶ search

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◉ **Adults and Teens with ADHD**

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- ◉ Important Safety Information
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Treating ADHD

Why ADHD treatment is important

Children and adolescents with Attention Deficit Hyperactivity Disorder (ADHD), if untreated, are at risk for poor academic performance. Teen pregnancy, problems with peers, car accidents, and physical injuries occur at a higher rate. Untreated, children and teens with ADHD are also at risk of conduct disorders, delinquency, and drug or alcohol abuse.

◉ **Focalin[®] XR**
(dexamethylphenidate hydrochloride) extended-release capsules last all day

◉ *Talk to a doctor before starting Focalin[®] XR (dexamethylphenidate hydrochloride) extended-release capsules*

Typically, adults with untreated ADHD experience academic hardships. These often start in childhood and are likely to worsen during college years. Untreated adults take longer to complete learning degrees. They are likely to have lower economic status, lower rates of employment, and more work-related problems. Untreated adults also have more problems in their relationships, more driving accidents, and more addiction—from alcohol to gambling.

Living with ADHD doesn't have to be this way. People with ADHD have treatment choices. The results of untreated ADHD are serious and should not be ignored. There is no cure for ADHD. Proper treatment can help control symptoms, helping to reduce these risks.

Sometimes, it takes more than 1 approach to treat all the symptoms of ADHD. A total ADHD treatment plan can help. It combines the use of medicines with other forms of therapy. This can enhance the benefits of taking drugs. It can help you function better.

Your total ADHD treatment plan

Your ADHD treatment plan may use standard medicines. You can also consider a host of alternative therapies. Your plan may include family and individual counseling and coaching. You can try behavior management or

For
Healthcare
Professionals

Focalin®
XR en
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to get your FREE
information-packed
"First Step for a Fast Start —
Living with ADHD"
guidebook

If you don't have prescription
coverage and can't afford
your medicines, visit:

www.pap.novartis.com
or call
1-800-245-5356

social skills training. Most important of all is educating yourself about the disorder.

The following sections give an overview of many things to consider as you put your personal plan together. Enlist the help of others as you make your plan. Consider people like a healthcare professional, family members, close friends, and coaches. It's all part of a team-based approach to your total ADHD treatment plan. It can provide far-reaching benefits to you and your whole family.

- **ADHD Behavior Management**
- **ADHD Counseling and Support**
- **ADHD Medical Treatments**

previous ◀ next ▶ **ADHD Behavior Management**

Focalin® XR (dexamethylphenidate HCl) extended-release capsules is indicated for the treatment of Attention Deficit Hyperactivity Disorder (ADHD) in adults, adolescents, and children 6 years and older with ADHD. Focalin® XR is available in 5, 10, 15, and 20 mg extended-release capsules. Focalin® XR is indicated as an integral part of a total treatment program for ADHD that may include other measures (eg, psychological, educational, social) for patients with this syndrome.

Important Safety Information

Focalin® XR should not be used if you have significant anxiety, tension, or agitation; allergies to methylphenidate; glaucoma, tics or Tourette's syndrome, or a family history of Tourette's syndrome; or if you have been taking an MAOI (a type of drug) or have discontinued an MAOI in the last 14 days.

Tell your doctor about any past or current heart problems that you or a family member has. If you have serious heart conditions, including structural heart abnormalities, you should generally not take stimulant drug products such as Focalin® XR. During treatment, tell your doctor if you develop any heart symptoms or conditions.

Tell your doctor if you have symptoms of depression, if you have been diagnosed with depression or bipolar disorder, or if you or a family member has a history of suicide, bipolar disorder, or depression. During treatment, tell your doctor if you develop any symptoms of depression or abnormal thoughts or behaviors.

Abuse of Focalin® XR can lead to dependence. Tell your doctor if you have ever abused or been dependent on alcohol or drugs, or if you are now abusing or dependent on alcohol or drugs.

Slower growth (weight gain and/or height) has been reported with long-term use of stimulants in children. Stimulants should be used with caution in patients with a prior history of seizures. Visual disturbances have been reported in patients taking methylphenidate.

See Full Prescribing Information

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