

Medicare Private Plans Urged to Prove Their Worth

BY JOEL B. FINKELSTEIN
Contributing Writer

WASHINGTON — If competition drives prices down, why does the government pay private insurers more per patient than the Medicare program spends on the average beneficiary?

That is the question on the minds of an increasing number of people, panelists pointed out at a press briefing on health care costs that was sponsored by the Cen-

ter for Studying Health System Change.

“A lot of folks are suffering from amnesia about this whole issue. In 2003, we passed something called the Medicare Modernization Act. ... It was about how are we going to solve the baby boomer problem, how are we going to bring Medicare costs under control,” said Robert Laszewski, president of a health policy and marketplace consulting firm in Alexandria, Va.

At the time, the Republican-led Con-

gress decided that the best way to bring costs under control was to encourage more Medicare beneficiaries to join private plans. So, depending upon which type of plan they offer, managed care companies receive 10%-20% above what Medicare spends on the average beneficiary in the government-run, fee-for-service system. This would induce private insurers to offer managed Medicare products and enable them to offer more benefits to attract beneficiaries into the

private plans, according to the philosophy behind the legislation.

It's 4 years later, Democrats are in power in Congress, and some are beginning to wonder what they are buying with the millions of extra dollars flowing to private insurers. Physician thought leaders, including those on the government's Medicare Physician Advisory Commission (MedPAC), have called for Congress to redirect those funds toward other priorities, such as fixing the sustainable growth rate formula.

However, it may be too early to pull the plug on this experiment in using private insurers to control costs, said Christine Arnold, a managing director at Morgan Stanley, where she covers the managed care industry. “The managed care companies that I speak to say that they can reduce medical costs 10% for a managed product versus an unmanaged product, but it takes 2-4 years,” she said.

It is not just in the Medicare program that the cost-saving techniques of managed care companies are being questioned.

Health savings accounts and other consumer-driven approaches are beginning to lose favor with the public. The number of U.S. workers who enrolled in consumer-directed plans grew by a meager 300,000 between 2005 and 2006, according to the Kaiser Family Foundation's annual survey of employer benefits.

A survey by America's Health Insurance Plans, a trade organization, seems to confirm that trend. After a couple of years in which enrollment in health savings account-affiliated, high-deductible plans doubled and then tripled, last year the number of people in the plans grew by less than a third.

Consumer-directed plans may be a good idea, but they're based on a false assumption that patients have the resources to make the right choices, said Douglas Simpson, the senior managed care analyst at Merrill Lynch & Co.

“We're incentivizing them with the benefit structure, but then we're really not giving them the tools to make better decisions. It's sort of like giving somebody \$100 to go out to dinner and then not putting the prices on the menu,” Mr. Simpson said.

The cyclical nature of health care reform also is becoming more apparent, said Joshua Raskin, who covers the managed care industry as a senior vice president at Lehman Brothers Inc.

During the late 1980s and early 1990s, health care premiums were growing by double digits. That resulted in a political backlash. At the time, it was Hillary Clinton's universal care plan that further popularized health maintenance organizations.

“HMOs had this huge period of proliferation and you got the cost trending down in the mid-1990s to ... really low single digits,” said Mr. Raskin. Then, the economy picked back up—and so did medical cost trends—and double-digit growth returned in the late 1990s into the early 2000s. Now, he said, the discussion is again focusing on “more government intervention. It's 2007 and 2008, and guess what: Hillary Clinton is back and so is universal health care.”

BRIEF SUMMARY: Consult the Full Prescribing Information for complete product information.
ADDERALL XR[®] CAPSULES *CF Rx Only*

ADDERALL XR[®] CAPSULES HAVE A HIGH POTENTIAL FOR ABUSE. ADMINISTRATION OF AMPHETAMINES FOR PROLONGED PERIODS OF TIME MAY LEAD TO DRUG DEPENDENCE. PARTICULAR ATTENTION SHOULD BE PAID TO THE POSSIBILITY OF SUBJECTS OBTAINING AMPHETAMINES FOR NON-THERAPEUTIC USE OR DISTRIBUTION TO OTHERS AND THE DRUGS SHOULD BE PRESCRIBED OR DISPENSED SPARINGLY. MISUSE OF AMPHETAMINE MAY CAUSE SUDDEN DEATH AND SERIOUS CARDIOVASCULAR ADVERSE EVENTS.

INDICATIONS
ADDERALL XR[®] is indicated for the treatment of Attention Deficit Hyperactivity Disorder (ADHD). The efficacy of ADDERALL XR[®] in the treatment of ADHD was established on the basis of two controlled trials in children aged 6 to 12, one controlled trial in adolescents aged 13 to 17, and one controlled trial in adults who met DSM-IV criteria for ADHD. Abuse with addiction from the known effect of ADDERALL XR[®], the immediate-release formulation of this substance.

CONTRAINDICATIONS
Advanced atherosclerosis, symptomatic cardiovascular disease, moderate to severe hypertension, hyperthyroidism, known hypersensitivity or idiosyncrasy to the sympathomimetic amines, glaucoma, agitated states. Patients with a history of drug abuse. During or within 14 days following the administration of monoamine oxidase inhibitors (hypertensive crisis may result).

WARNINGS
Serious Cardiovascular Events
Sudden Death and Pre-existing Structural Cardiac Abnormalities or Other Serious Heart Problems
Children and Adolescents
Sudden death has been reported in association with CNS stimulant treatment at usual doses in children and adolescents with structural cardiac abnormalities or other serious heart problems. Although some serious heart problems alone carry an increased risk of sudden death, stimulant products generally should not be used in children or adolescents with known serious structural cardiac abnormalities, cardiomyopathy, serious heart rhythm abnormalities, coronary artery disease, or other serious cardiac conditions that may place them at increased vulnerability to the sympathomimetic effects of a stimulant drug (see CONTRAINDICATIONS).
Adults
Sudden death, stroke, and myocardial infarction have been reported in adults taking stimulant drugs at usual doses for ADHD. Although the role of stimulants in these adult cases is also unknown, adults have a greater likelihood than children of having serious structural cardiac abnormalities, cardiomyopathy, serious heart rhythm abnormalities, coronary artery disease, or other serious cardiac conditions. Adults with such abnormalities should also generally not be treated with stimulant drugs (see CONTRAINDICATIONS).

Hypertension and other Cardiovascular Conditions
Stimulant medications cause a modest increase in average blood pressure (about 2-4 mmHg) and average heart rate (about 3-6 bpm) (see ADVERSE EVENTS), and individuals may have larger increases. While the mean changes alone would not be expected to have short-term consequences, all patients should be monitored for larger changes in heart rate and blood pressure. Caution is indicated in treating patients whose underlying medical conditions might be compromised by increases in blood pressure or heart rate, e.g., those with pre-existing hypertension, heart failure, recent myocardial infarction, or ventricular arrhythmias (see CONTRAINDICATIONS).

Psychiatric Adverse Events
Pre-existing Psychosis
Administration of stimulants may exacerbate symptoms of behavior disturbance and thought disorder in patients with pre-existing psychotic disorder.

Bipolar Illness
Particular care should be taken in using stimulants to treat ADHD patients with comorbid bipolar disorder because of concern for possible manic episode in such patients. Prior to initiating treatment with a stimulant, patients with comorbid depressive symptoms should be adequately screened to determine if they are at risk for bipolar disorder, since screening should include a detailed psychiatric history, including a family history of suicide, bipolar disorder, and depression. Emergence of Manic Psychotic or Manic Symptoms
Treatment emergent psychotic or manic symptoms, e.g., hallucinations, delusional thinking, or mania in children and adolescents without prior history of psychotic illness or mania can be caused by stimulants at usual doses. If such symptoms occur, consideration should be given to a possible causal role of the stimulant, and discontinuation of treatment may be appropriate. In a pooled analysis of multiple short-term, placebo-controlled studies, such symptoms occurred in about 3.1% (4 patients with events out of 3482 exposed to methylphenidate or amphetamine for several weeks at usual doses) of stimulant-treated patients compared to 0 in placebo-treated patients.

Aggression
Aggressive behavior or hostility is often observed in children and adolescents with ADHD, and has been reported in clinical trials. After the beginning of exposure to stimulant medication for the treatment of ADHD, there is no systematic evidence that stimulants cause aggressive behavior or hostility. Patients beginning treatment for ADHD should be monitored for the appearance of or worsening of aggressive behavior or hostility.

Long-Term Suppression of Growth
Careful follow-up of weight and height in children aged 7 to 10 years who were randomized to either methylphenidate or non-medication treatment groups over 14 months, as well as in retrospective subgroups of newly methylphenidate-treated and non-medication treated children over 30 months (to the ages of 10 to 13 years), suggests that consistently medicated children (i.e., treatment for 7 days per week throughout the year) have a temporary slowing in growth rate (an average, a total of about 2 cm less growth in height and 2.7 kg less growth in weight over 3 years), without evidence of growth rebound during the initial 4 weeks of therapy was -1.1 lbs. And -2.8 lbs., respectively, for patients receiving 10 mg and 20 mg ADDERALL XR[®]. Higher doses were associated with greater weight loss within the initial 4 weeks of treatment. Published data are inadequate to determine whether chronic use of amphetamines may cause a similar suppression of growth, however, it is anticipated that they will have a similar effect. Therefore, growth should be monitored during treatment with stimulants, and patients who are not growing or gaining weight as expected may need to have their treatment interrupted.

Seizures
There is some clinical evidence that stimulants may lower the convulsive threshold in patients with prior history of seizures, in patients with prior EEG abnormalities in absence of seizures, and very rarely, in patients without a history of seizures and no prior EEG evidence of seizures. In the presence of seizures, the drug should be discontinued.

Visual Disturbance
Difficulties with accommodation and blurring of vision have been reported with stimulant treatment.

PRECAUTIONS
General: The least amount of amphetamine feasible should be prescribed or dispensed at one time in order to minimize the possibility of overdose. ADDERALL XR[®] should be used with caution in patients who use other sympathomimetic drugs.

Toxicity: Amphetamines have been reported to exacerbate motor and phoric tics and Tourette's syndrome. Therefore, clinical evaluation for tic and Tourette's syndrome is advised and the families should be made aware of stimulant medication.

Information for Patients: Amphetamines may impair the ability of the patient to engage in potentially hazardous activities such as operating machinery or vehicles; the patient should therefore be cautioned accordingly.

Drug Interactions: Acetylcholinesterase inhibitors—Anticholinergic agents (antispasmodics, atropine, glycopyrrate, scopolamine, donepezil, galantamine, tacrine, rivastigmine, etc.) lower absorption of amphetamines. Opioid analgesic agents—These agents (meperidine, butorphanol, buprenorphine, fentanyl, etc.) increase the concentration of the amphetamine enantiomer, thereby increasing urinary excretion. Both groups of agents lower blood levels and efficacy of amphetamines. Adrenergic blockers—Adrenergic blockers are inhibited by amphetamines. Amphetamines may impair the ability of the patient to engage in potentially hazardous activities such as operating machinery or vehicles; the patient should therefore be cautioned accordingly.

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Drug/Laboratory Test Interactions: Amphetamines may cause a significant elevation in plasma corticosteroid levels. This increase is greatest in the evening. Amphetamines may interfere with urinary steroid determinations.
Diagnosis/Management and Laboratory Tests: No evidence of carcinogenicity was found in studies in which d,l-amphetamine (enantiomer ratio of 1:1) was administered to mice and rats in the diet for 2 years at doses of up to 38 mg/kg/day in male mice, 18 mg/kg/day in female mice, and 5 mg/kg/day in male and female rats. These doses are approximately 2.4, 1.5, and 0.8 times, respectively, the maximum recommended human dose of 30 mg/kg [300 mg] on a mg/m² body surface area basis.
Amphetamines: In the enantiomer ratio present in ADDERALL XR[®] (immediate-release) (d- to l- ratio of 3:1), was not diastereic in the same dose manner interaction test in vivo and was negative when tested in the 2'-OH component of the Ames test in vivo. d,l-Amphetamine (1:1 enantiomer ratio) has been reported to produce a positive response in the mouse bone marrow micronucleus test, an equivocal response in the Ames test, and negative responses in the in vivo sister chromatid exchange and chromosome aberration assays.
Amphetamine: In the enantiomer ratio present in ADDERALL XR[®] (immediate-release) (d- to l- ratio of 3:1), did not adversely affect fertility or early embryonic development in the rat at doses of up to 30 mg/kg/day (approximately 5 times the maximum recommended human dose of 30 mg/kg/day on a mg/m² body surface area basis).
Pregnancy: Pregnancy Category C. Amphetamines are present in ADDERALL XR[®] (d- to l- ratio of 3:1), had no apparent effects on embryonal morphological development or survival when orally administered to pregnant rats and rabbits throughout the period of organogenesis at doses of up to 6 and 18 mg/kg/day, respectively. These doses are approximately 1.5 and 4.5 times, respectively, the maximum recommended human dose of 30 mg/kg/day [300 mg] on a mg/m² body surface area basis. Fetal malformations and death have been reported in mice following parental administration of d-amphetamine doses of 50 mg/kg/day (approximately 6 times that of a human dose of 30 mg/kg/day [300 mg] on a mg/m² body surface area basis) or greater to pregnant animals. Administration of these doses may also be associated with severe maternal toxicity.
Abuse: A number of studies in rodents indicate that perinatal or early postnatal exposure to amphetamine (d- or d,l-) at doses similar to those used clinically, can result in long-term neurochemical and behavioral alterations. Reported behavioral effects include learning and memory deficits, altered locomotor activity, and changes in sexual function.

There are no adequate and well-controlled studies in pregnant women. There has been one report of severe congenital bony deformity, tracheo-esophageal fistula, and nasal abductor (craniofacial) in a baby born to a woman who took dextroamphetamine sulfate with levodopa during the first trimester of pregnancy. Amphetamines should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.
Neuroleptic Effects: Infants born to mothers dependent on amphetamines have an increased risk of premature delivery and low birth weight. Also, these infants may experience symptoms of withdrawal as demonstrated by dysphoria, including agitation, and significant irritability.
Usage in Nursing Mothers: Amphetamines are excreted in human milk. Mothers taking amphetamines should be advised to refrain from nursing.
Pediatric Use: ADDERALL XR[®] is indicated for use in children 6 years of age and older.
Use in Children Under Six Years of Age: Effects of ADDERALL XR[®] in 3-5 year olds have not been studied. Long-term effects of amphetamines in children have not been well established. Amphetamines are not recommended for use in children under 3 years of age.
Geriatric Use: ADDERALL XR[®] has not been studied in the geriatric population.

ADVERSE EVENTS
Hypertension (see WARNINGS section) In a controlled 4-week outpatient clinical study of adolescents with ADHD, isolated systolic blood pressure elevations ≥15 mmHg were observed in 754 (11%) placebo-treated patients and 713 (7%) patients receiving ADDERALL XR[®] 10 or 20 mg. Isolated elevations in diastolic blood pressure ≥ 8 mmHg were observed in 1664 (25%) placebo-treated patients and 23/100 (23%) ADDERALL XR[®] treated patients. Similar results were observed at higher doses. In a single-dose pharmacokinetic study in 23 adolescents, isolated increases in systolic blood pressure (above the upper 95% CI for age, gender and stature) were observed in 2/17 (12%) and 8/23 (35%), subjects administered 10 mg and 20 mg ADDERALL XR[®], respectively. Higher single doses were associated with a greater increase in systolic blood pressure. All increases were transient, appeared within 2 to 4 hours post-dose and not associated with symptoms. The pre-linguistic development program for ADDERALL XR[®] included exposures in a total of 1215 participants in clinical trials (835 pediatric patients, 358 adolescent patients, 242 adult patients, 82 healthy adult subjects). Of these, 835 patients (ages 6 to 12) were evaluated in two controlled clinical studies, an open-label clinical study, and two single-dose clinical pharmacology studies (N=46). Safety data on all patients are included in the discussion that follows. Adverse reactions were assessed by collecting adverse events, results of physical examinations, vital signs, weights, laboratory analyses, and ECGs. Adverse events during exposure were obtained primarily by general inquiry and recorded by clinical investigators using terminology of their own choosing. Consequently, it is not possible to provide a meaningful estimate of the proportion of individuals experiencing adverse events without first grouping similar types of events into a smaller number of standardized event categories. In the tables and listings that follow, COASTAL terminology has been used to clearly report adverse events. The stated frequencies of adverse events represent the proportion of individuals who experienced, at least once, a treatment-emergent adverse event of the type listed.
Adverse events associated with discontinuation of treatment: In two placebo-controlled studies of up to 5 weeks duration among children with ADHD, 2.4% (70/425) of ADDERALL XR[®] treated patients discontinued due to adverse events (including 3 patients with loss of appetite, one of whom also reported insomnia) compared to 2.1% (7/258) receiving placebo. The most frequent adverse events associated with discontinuation of ADDERALL XR[®] in controlled and uncontrolled, multiple-dose clinical trials of pediatric patients (N=595) are presented below. Over half of these patients were exposed to ADDERALL XR[®] for 12 weeks or more.

Adverse Event	% of Pediatric Patients (N=595)
Anorexia (loss of appetite)	2.9
Insomnia	1.5
Weight loss	1.2
Central Nervous System Irritability	1.0
Depression	0.7

In women, 1% (n=2) each for headache, palpitation, and somnolence, and, 0.5% (n=1) each for ALT increase, agitation, chest pain, cocaine craving, elevated blood pressure, and weight loss.
Adverse events occurring in a controlled trial: Adverse events reported in a 3-week clinical trial of pediatric patients and a 4-week clinical trial in adolescents and adults, respectively, treated with ADDERALL XR[®] or placebo are presented in the tables below. The prescriber should be aware that these figures cannot be used to predict the incidence of adverse events in the course of usual medical practice where patient characteristics and other factors differ from those which prevailed in the clinical trials. Similarly, the cited frequencies cannot be compared with figures obtained from other clinical investigations involving different treatments, uses, and investigations. The cited figures, however, do provide the prescribing physician with some basis for estimating the relative contribution of drug and non-drug factors to the adverse event incidence rate in the population studied.

The following adverse reactions have been associated with the use of amphetamine, ADDERALL XR[®], or ADDERALL XR[®]:
Cardiovascular: Palpitations, tachycardia, elevation of blood pressure, sudden death, myocardial infarction. There have been isolated reports of cardiomyopathy associated with chronic amphetamine use.
Central Nervous System: Psychotic episodes (recommended doses), overstimulation, restlessness, dizziness, insomnia, euphoria, dysphoria, dysthymia, depression, anxiety, headache, exacerbation of motor and phoric tics and Tourette's syndrome, seizures, stroke.
Gastrointestinal: Dryness of the mouth, unpleasant taste, diarrhea, constipation, other gastrointestinal disturbances. Anorexia and weight loss may occur as undesirable effects.

Allergic: Urticaria, rash, hypersensitivity reactions (fever, angioedema, and anaphylaxis). Serious skin reactions including Stevens-Johnson Syndrome and toxic epidermal necrolysis have been reported.
Endocrine: Impotence, changes in libido.
Tolerance, extreme psychological dependence, and severe social disability have occurred. There are reports of patients who have increased the dosage to levels many times higher than recommended. Abrupt cessation following prolonged high-dose use may result in extreme fatigue and mental depression; changes are also noted on the sleep EEG. Manifestations of chronic intoxication with amphetamines may include severe dermatoses, marked insomnia, irritability, hyperactivity, and personality changes. The most severe manifestation of chronic intoxication is psychosis, often clinically indistinguishable from schizophrenia.

OVERDOSE
Individual patient response to amphetamines varies widely. Toxic symptoms may occur idiosyncratically at low doses.
Symptoms: Manifestations of acute overdose include: hyperreflexia, hyperextension of the neck, hyperreflexia, rapid respiration, confusion, assaultiveness, hallucinations, panic states, hyperpyrexia and rhabdomyolysis, fatigue and depression usually follow the central nervous system stimulation. Cardiovascular effects include tachycardia, hypertension and hypotension and circulatory collapse. Gastrointestinal symptoms include nausea, vomiting, diarrhea, and abdominal cramps. Fatal poisoning is usually preceded by convulsions and coma.
Treatment: Consult with a Certified Poison Control Center for up to date guidance and advice. Management of acute amphetamine intoxication is largely symptomatic and includes gastric lavage, administration of activated charcoal, administration of a cathartic and sedation. Experience with hemodialysis or peritoneal dialysis is inadequate to permit recommendation in this regard. Administration of the urine increases amphetamine excretion, but is believed to increase risk of acute renal failure if hypotension is present. If acute severe hyperreflexia complicates amphetamine overdose, administration of intravenous phenothiazine has been suggested. However, a gradual drop in blood pressure will usually result when sufficient sedation has been achieved. Chlorpromazine antagonizes the central stimulant effects of amphetamines and can be used to treat amphetamine intoxication. The procedure of choice for the management of acute amphetamine overdose should be considered when treating patients with overdose.

Dispose in a light, light-resistant container as defined in the USP. Store at 25° C (77° F). Excursions permitted to 15-30° C (59-86° F) [see USP Controlled Room Temperature].
Manufactured for: **Shire US Inc.**, Wayne, PA 19087
Made in USA For more information call 1-800-829-3288, or visit www.adderall.com.
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Table 1: Adverse Events Reported by More Than 1% of Pediatric Patients Receiving ADDERALL XR[®] with Higher Incidence Than on Placebo in a 52-Week Clinical Study

Body System	Preferred Term	ADDERALL XR [®] (n=216)	Placebo (n=218)
General	Abdominal Pain (abdominal)	14%	10%
	Headache	3%	2%
	Accidental Injury	2%	2%
	Asthenia (fatigue)	2%	2%
	Fever	2%	2%
Digestive System	Loss of Appetite	22%	2%
	Dyspepsia	2%	1%
	Nausea	2%	2%
Nervous System	Dizziness	2%	2%
	Emotional Lability	3%	2%
Metabolic/Nutritional	Insomnia	17%	2%
	Nervousness	8%	2%
	Weight Loss	4%	2%

Table 2: Adverse Events Reported by 5% or more of Adolescents (weighing > 75 lbs) Receiving ADDERALL XR[®] with Higher Incidence Than Placebo in a 26-Week Clinical Study

Body System	Preferred Term	ADDERALL XR [®] (n=231)	Placebo (n=24)
General	Abdominal Pain (abdominal)	11%	2%
	Headache	6%	1%
Digestive System	Loss of Appetite	30%	2%
	Diarrhea	6%	2%
Nervous System	Insomnia	12%	4%
	Nervousness	6%	0%
Metabolic/Nutritional	Weight Loss	8%	0%

Table 3: Adverse Events Reported by 5% or more of Adults Receiving ADDERALL XR[®] with Higher Incidence Than on Placebo in a 26-Week Clinical Study

Body System	Preferred Term	ADDERALL XR [®] (n=91)	Placebo (n=44)
General	Headache	26%	12%
	Insomnia	6%	2%
	Nausea	2%	2%
Digestive System	Loss of Appetite	22%	2%
	Diarrhea	6%	2%
	Nausea	2%	2%
	Dyspepsia	2%	2%
Nervous System	Agitation	8%	5%
	Anxiety	8%	5%
	Dizziness	7%	8%
Cardiovascular System	Tachycardia	8%	2%
	Weight Loss	11%	0%
Urinary System	Urinary Tract Infection	5%	0%

* Approx. 1 hour due to vomiting
† Case-related adverse events
Note: The following events did not meet the criteria for inclusion in Table 3 but were reported by 2% to 4% of adolescent patients receiving ADDERALL XR[®] with a higher incidence than placebo receiving placebo in this study: accidental injury, asthenia, fatigue, dry mouth, dyspepsia, emotional lability, nausea, nervousness, and vomiting.
* Included doses up to 60 mg.
Note: The following events did not meet the criteria for inclusion in Table 3 but were reported by 2% to 4% of adult patients receiving ADDERALL XR[®] with a higher incidence than placebo receiving placebo in this study: infection, photosensitivity reaction, somnolence, tooth disorder, emotional lability, taste decreased, somnolence, speech disorder, palpitation, twinning, dizziness, twinning, dyspareunia, and impotence.
* Included doses up to 60 mg.