

Government to Monitor EHR Adoption Gap

BY ELAINE ZABLOCKI
Contributing Writer

SAN DIEGO — Government strategies for health information technology will aid physicians by lowering the cost, improving the benefits, and lowering the risks, said David J. Brailer, M.D., Ph.D., national coordinator for health information technology, in a keynote address at the annual meeting of the American Health Lawyers Association.

Information technology "is a tectonic issue for physicians, one that separates old from young, progressive from Luddite, and those who want to be part of a performance-based future from those who want to practice the way they have for years," said Dr. Brailer of the Department of Health and Human Services, Washington. "We're trying to be nonregulatory, to use a market-based approach, and that means we want to work with the willing. Surveys show that many physicians, at

least half today, would do this if they could figure out how to do it."

One barrier to adoption of electronic health records (EHRs) is the variety of products on the market. Certifying a basic, minimally featured EHR system will aid physicians in making rational purchasing decisions, Dr. Brailer said.

Another barrier to adoption of EHRs is the current lack of a sound business model. A "pay-as-you-go" financial model is not feasible, and financial incentives will be

needed to accelerate the transition, Dr. Brailer said, without specifying any further details.

Large physician groups and hospitals are far ahead of small physician offices in adopting EHRs. According to Jodi Goldstein Daniel, a Department of Health and Human Services senior staff attorney on health information technology issues who also spoke at the meeting, more than 50% of large practices have adopted EHRs, while only 13% of small practices have done so. Dr. Brailer's office plans to monitor the adoption gap annually, to see whether it is closing, whether certified technologies are being used, and whether rural practices and other practices with special needs require some kind of safety net.

"We don't want to see health IT become a strategic wedge between the haves and the have-nots," Dr. Brailer said. "We want a level playing field so that everyone can participate." ■

References: 1. Faraone SV, Biederman J. A controlled study of functional impairments in 500 ADHD adults. Presented at: 157th Annual Meeting of the American Psychiatric Association; May 5, 2004; New York, NY. 2. Data on file, Shire US Inc., 2005. 3. ADDERALL XR® [package insert], Shire US Inc., 2005. 4. Claxton AJ, Cramer J, Pierce C. A systematic review of the association between dose regimens and medication compliance. *Clin Ther.* 2001;23:1296-1310.

BRIEF SUMMARY: Consult the full prescribing information for complete product information.

ADDERALL XR® CAPSULES
CII Rx Only

AMPHETAMINES 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.

DISUSE 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, along with extrapolation from the known efficacy of ADDERALL®; the immediate-release formulation of this substance.

CONTRAINDICATIONS:

Advanced arteriosclerosis, 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 (hypomanic crises may result).

WARNINGS:

Psychosis: Clinical experience suggests that, in psychotic patients, administration of amphetamine may exacerbate symptoms of behavior disturbance and thought disorder.

Long-Term Suppression of Growth: Data are inadequate to determine whether chronic use of stimulants in children, including amphetamine, may be causally associated with suppression of growth. Therefore, growth should be monitored during treatment, and patients who are not growing or who weight gain is observed should have their treatment re-evaluated.

Sudden Death and Pre-existing Structural Cardiac Abnormalities: Sudden death has been reported in association with amphetamine treatment at usual doses in children with structural cardiac abnormalities. Adderall XR® generally should not be used in children, adolescents, or adults with structural cardiac abnormalities.

PRECAUTIONS:

General: The least amount of amphetamine feasible should be prescribed or dispensed at one time in order to minimize the possibility of overdose.

Hypertension: Caution is to be exercised in prescribing amphetamines for patients with even mild hypertension (see CONTRAINDICATIONS). Blood pressure and heart rate should be monitored at appropriate intervals in patients taking ADDERALL XR®. Patients with a history of hypertension.

Sustained Increases in Blood Pressure: Sustained increases in blood pressure should be treated with dose reduction and/or appropriate medication.

In a controlled 4-week outpatient clinical study of adolescents with ADHD, isolated systolic blood pressure elevations ≥15 mmHg were observed in 7/64 (11%) placebo-treated patients and 7/100 (7%) patients receiving ADDERALL XR® 0.05 or 20 mg. Isolated elevations in diastolic blood pressure ≥ 8 mmHg were observed in 16/64 (25%) placebo-treated patients and 22/100 (22%) 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% age- and gender-specific limit) (12%) and diastolic blood pressure (above the upper 95% age- and gender-specific limit) (10 mg and 20 mg ADDERALL XR®, respectively). Higher single doses were associated with a greater increase in systolic blood pressure.

Tics: Amphetamines have been reported to exacerbate motor and phonic tics and Tourette's syndrome. Therefore, clinical evaluation for tics and Tourette's syndrome in children and their families should precede use of stimulant medications.

Effects on Weight: Amphetamines have been associated with decreased appetite. Absolute weight increases in treated children over time, but the increases are smaller than expected based on CDC normative values. These reductions in weight over time attenuate over time and are greatest in the heaviest children. In the controlled trial in adolescents, mean weight change from baseline within the initial 4 weeks of treatment was -1.1 lbs. and -2.2 lbs., respectively, for patients receiving 10 mg and 20 mg ADDERALL XR®. Higher doses should be associated with greater weight loss than within the initial 4 weeks of treatment.

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: **Acidifying agents—Gastrointestinal acidifying agents:** (guanethidine, reserpine, glutamic acid HCl, ascorbic acid, etc.) may cause absorption of amphetamines. **Urinary acidifying agents:** These agents (ammonium chloride, sodium bicarbonate, etc.) inhibit the conversion of the amphetamine molecule, thereby increasing urinary excretion. Both groups of agents lower blood levels and efficacy of amphetamines. **Adrenergic blockers—Adrenergic blockers:** Adrenergic blockers are inhibited by amphetamines. **Gastrointestinal alkalinizing agents:** (sodium bicarbonate, etc.) increase absorption of amphetamines. Co-administration of ADDERALL XR® and gastrointestinal alkalinizing agents, such as antacids, should be avoided. Urinary alkalinizing agents (acetazolamide, some thiazides) increase the concentration of the non-ionized species of the amphetamine molecule, thereby decreasing urinary excretion. Both groups of agents increase blood levels and therefore potentiate the actions of amphetamines. **Antidepressants—Tricyclics—Amitriptyline:** Amitriptyline increases the activity of amphetamines and may potentiate their effects with desipramine or propantheline and possibly other tricyclics cause striking and sustained increases in the concentration of d-amphetamine in the brain. **Cardiovascular:** Amphetamines can be potentiated by MAO inhibitors—MAO inhibitors, as well as a metabolite of furazolidone, slow amphetamine metabolism. This slowing potentiates amphetamines, increasing their effect on the release of norepinephrine and other monoamines from adrenergic nerve endings; this can cause headaches and other signs of hypertension crisis. A variety of toxic neurological effects and malignant hypertension can occur, sometimes with fatal results. **Antihistamines:** Amphetamines may counteract the sedative effect of antihistamines. **Antihistamines—tricyclics—Amphetamine:** Amphetamine may antagonize the sedative effect of certain antihistamines. **Anticholinergics:** Amphetamine may antagonize the anticholinergic effect of certain anticholinergics. **Cholinergics:** Cholinergics may block treat amphetamine poisoning. **Ethoxzolamide—Amphetamines:** May delay intestinal absorption of ethoxzolamide. **Haloperidol—Haloperidol blocks dopamine receptors, thus inhibiting the central stimulant effects of amphetamines. Lithium carbonate—**The anorectic and stimulatory effects of amphetamines may be inhibited by lithium carbonate. **Meperidine—**Amphetamines potentiate the analgesic effect of meperidine. **Methenamine therapy—**Urinary excretion of amphetamines is increased, and efficacy is reduced, by activating agents used in methenamine therapy. **Norepinephrine—**Amphetamines may enhance the adrenergic effects of norepinephrine. **Phenothiazines:** Phenothiazines may antagonize the anticholinergic effect of amphetamines. **Phenothiazines—**Co-administration of phenothiazines may produce a synergistic anticonvulsant action. **Phenytoin:** Amphetamines may delay intestinal absorption of phenytoin; co-administration of phenytoin may produce a synergistic anticonvulsant action. **Propoxyphene:** In cases of propoxyphene overdose, amphetamine CNS stimulation is potentiated and fatal convulsions can occur. **Veratrum alkaloids—**Amphetamines inhibit the hypotensive effect of veratrum alkaloids. **Drug/Laboratory Test Interactions:** Amphetamines can cause a significant elevation in plasma corticosteroid levels. This increase is greatest in the evening. Amphetamines may interfere with urinary steroid determinations.

Carcinogenesis/Mutagenesis and Impairment of Fertility: No evidence of carcinogenicity was found in studies in which amphetamines were administered to mice and rats. No evidence of mutagenicity was found in Ames test at doses of up to 30 mg/kg/day in male mice, 19 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/day [child] on a mg/m² basis or surface area basis.

Amphetamine, in the enantiomer ratio present in ADDERALL® (immediate-release) (d- to l- ratio of 3:1), was not clastogenic in the mouse bone marrow micronucleus test and was negative when tested in the *E. coli* component of the Ames test. *In vitro* d-l-amphetamine enantiomer ratio has been reported to produce a positive response in the mutagenicity test, an epoxidase test, and a sister chromatid exchange and chromosomal aberration assays.

Amphetamine, in the enantiomer ratio present in ADDERALL® (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 20 mg/kg/day (approximately 5 times the maximum recommended human dose of 30 mg/day on a mg/m² body surface area basis).

Pregnancy: Pregnancy Category C. Amphetamine, in the enantiomer ratio present in ADDERALL® (d- to l- ratio of 3:1), had no apparent effect on embryo development or fetal growth in the rat. There is no information on the use of amphetamine in pregnant women.

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 anal atresia (water association) in a baby born to a woman who took dextroamphetamine sulfate with lovastatin during the first trimester of pregnancy. Amphetamines should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nonteratogenic 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

abnormal behavior, irritability, and significant lassitude.

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:

The initial development program for ADDERALL XR® included 1000 subjects in a total of 1315 participants in clinical trials (639 pediatric patients, 350 adolescent patients, 249 adult healthy adult subjects). Of these, 635 patients

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The following adverse events did not meet the criterion for inclusion in Table 2 but were reported by 2% to 4% of adolescent patients taking ADDERALL XR® with a higher incidence than patients receiving placebo in this study: accidental injury, asthenia (fatigue), dry mouth, dyspepsia, emotional lability, nausea, somnolence, and vomiting.

Table 1. Adverse Events Reported by More Than 1% of Pediatric Patients Receiving ADDERALL XR® with Higher Incidence Than on Placebo in a 584 Patient Clinical Study

Body System	Preferred Term	ADDERALL XR® (n=374)	Placebo (n=210)
General	Abdominal Pain (stomachache)	14%	10%
	Accidental Injury	3%	2%
	Asthenia (fatigue)	2%	0%
	Fever	5%	2%
	Infection	4%	2%
	Viral Infection	2%	0%
Digestive System	Loss of Appetite	22%	2%
	Diarrhea	2%	1%
	Dyspepsia	2%	1%
	Nausea	5%	3%
	Vomiting	7%	4%
Nervous System	Dizziness	2%	0%
	Emotional Lability	9%	2%
	Insomnia	17%	2%
	Nervousness	6%	2%
Metabolic/Nutritional	Weight Loss	4%	0%

Table 2. Adverse Events Reported by 5% or More of Adolescents Weighing ≤ 75 kg/165 lbs Receiving ADDERALL XR® with Higher Incidence Than Placebo in a 287 Patient Clinical Forced Weekly-Dose Titration Study*