

# Mass. Curtails Free Vaccines for Older Children

BY JANE ANDERSON  
Contributing Writer

Massachusetts health authorities, facing huge demands for vaccines to prevent meningitis, diphtheria/tetanus/pertussis, and chickenpox, have asked the state's pediatricians to limit use of the shots in older children under the state's free vaccine program.

Although state officials said that no child will go without needed vaccines, pe-

diatricians in Massachusetts said the shortage, plus a state decision last year not to cover the quadrivalent human papillomavirus vaccine (Gardasil), marks the end of the state's universal vaccination program, and is leading to additional red tape for them.

Previously, Massachusetts provided all childhood vaccinations for every child, regardless of insurance coverage or coverage by the joint federal-state Vaccines for Children (VFC) program. In the past, as shots

were added, the state Department of Public Health (DPH) typically bought enough vaccine stock to cover the children in the age group recommended, plus a bit more to help older children "catch up," DPH spokeswoman Donna Rheume said in an interview.

Massachusetts has been in the forefront of states that buy vaccines for children and then distribute them to physicians, and will spend about \$40 million this year to buy pediatric vaccines, she said.

But this year, the state has seen unprecedented demand for three vaccines—conjugate meningococcal vaccine (MCV4) (Menactra), tetanus-diphtheria acellular pertussis (Tdap; Adacel or Boostrix), and varicella vaccine (Varivax), Ms. Rheume said. Therefore, there is only enough vaccine left to cover seventh-graders, the group that is routinely given the shots.

"The only change now is that providers will have to bill the insurance companies for non-VFC-eligible children—children who have private health insurance," said Ms. Rheume. There are no plans to buy additional vaccine doses, she said, adding that "in 5 years, we anticipate all children will have received these vaccines."

But Massachusetts insurers are not set up to pay for childhood vaccines because the state has provided them for free until now, said Dr. David Link, chief of pediatricians at Cambridge Health Alliance. "What was taken for granted—that all children would have full access to vaccines—that compact has now disappeared," he said in an interview.

"We're now creating disparities we never have had before," added Dr. Sean Palfrey, professor of pediatrics at Boston University and former president of the Massachusetts chapter of the American Academy of Pediatrics.

Both Dr. Palfrey and Dr. Link said that pediatricians are facing huge paperwork hurdles to prove children are eligible for the free federal-state program, and that they also have to make sure to chase down doses of the three vaccines in question for children whose vaccinations now must be paid for by private insurance companies.

The reason for the changes in state policy is the much higher cost of newer vaccines, such as Menactra and Gardasil, said Dr. Link.

In fact, he said, the decision by the Massachusetts legislature in 2007 not to cover the HPV vaccine—which would have cost up to \$14 million a year—marked the end of the last state program that provided free, universal vaccinations. Despite heavy lobbying of Massachusetts lawmakers by physicians and children's advocates, there currently are not enough votes to reverse the decisions to curtail the vaccine program, he said.

Eventually, there will be outbreaks of preventable disease, Dr. Link predicted: "Some kid is going to wind up very damaged or dead because of this, because we decided we preferred some more asphalt [instead of] protecting kids."

**Vyvanse™ (lisdexamfetamine dimesylate)** CII Rx Only

**BRIEF SUMMARY:** Consult the Full Prescribing Information for complete product information.

**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.**

**MISUSE OF AMPHETAMINE MAY CAUSE SUDDEN DEATH AND SERIOUS CARDIOVASCULAR ADVERSE EVENTS.**

**INDICATIONS AND USAGE**  
Vyvanse is indicated for the treatment of Attention-Deficit/Hyperactivity Disorder (ADHD). The efficacy of Vyvanse in the treatment of ADHD was established on the basis of two controlled trials in children aged 6 to 12, who met DSM-IV criteria for ADHD (see CLINICAL TRIALS).

A diagnosis of Attention-Deficit/Hyperactivity Disorder (ADHD; DSM-IV<sup>®</sup>) implies the presence of hyperactive-impulsive or inattentive symptoms that caused impairment and were present before age 7 years. The symptoms must cause clinically significant impairment in social, academic, or occupational functioning, and be present in two or more settings, e.g., at school (or work) and at home. The symptoms must not be better accounted for by another mental disorder. For the inattentive type, at least six of the following symptoms must have persisted for at least 6 months: lack of attention to details/careless mistakes; lack of sustained attention; poor listener; failure to follow through on tasks; poor organization; avoids tasks requiring sustained mental effort; loses things; easily distracted; forgetful. For the hyperactive-impulsive type, at least six of the following symptoms must have persisted for at least 6 months: fidgeting/squirming; leaving seat; inappropriate running/climbing; difficulty with quiet activities; "on the go"; excessive talking; blurting answers; can't wait turn; intrusive. The Combined Type requires both inattentive and hyperactive-impulsive criteria to be met.

**Special Diagnostic Considerations:** Specific etiology of this syndrome is unknown, and there is no single diagnostic test. Adequate diagnosis requires the use not only of medical but also of special psychological, educational, and social resources. Learning may or may not be impaired. The diagnosis must be based upon a complete history and evaluation of the child and not solely on the presence of the required number of DSM-IV<sup>®</sup> characteristics.

**Need for Comprehensive Treatment Program:** Vyvanse 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. Drug treatment may not be indicated for all children with this syndrome. Stimulants are not intended for use in the child who exhibits symptoms secondary to environmental factors and/or other primary psychiatric disorders, including psychosis. Appropriate educational placement is essential and a psychosocial intervention is often needed. When remedial measures alone are insufficient, the decision to prescribe stimulant medication will depend upon the physician's assessment of the chronicity and severity of the child's symptoms.

**Long-Term Use:** The effectiveness of Vyvanse for long-term use, i.e., for more than 4 weeks, has not been systematically evaluated in controlled trials. Therefore, the physician who elects to use Vyvanse for extended periods should periodically re-evaluate the long-term usefulness of the drug for the individual patient.

**CONTRAINDICATIONS**  
Advanced arteriosclerosis, symptomatic cardiovascular disease, moderate to severe hypertension, hyperthyroidism, known hypersensitivity or idiosyncrasy to the sympathomimetic amines, glaucoma.

**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 and/or other serious heart problems. Some of these children also 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, or other serious cardiac problems that may place them at increased vulnerability to the sympathomimetic effects of a stimulant drug (see CONTRAINDICATIONS).

Adults  
Sudden deaths, 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 pre-existing structural cardiac abnormalities, cardiomyopathy, serious heart rhythm abnormalities, coronary artery disease, or other serious cardiac problems. 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), 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 arrhythmia (see CONTRAINDICATIONS).

**Assessing Cardiovascular Status in Patients being Treated with Stimulant Medications**  
Children, adolescents, or adults who are being considered for treatment with stimulant medications should have a careful history (including assessment for a family history of sudden death or ventricular arrhythmia) and physical exam to assess for the presence of cardiac disease, and should receive further cardiac evaluation if findings suggest such disease (e.g., electrocardiogram and echocardiogram). Patients who develop symptoms such as unexplained chest pain, unexplained syncope, or other symptoms suggestive of cardiac disease during stimulant treatment should undergo a prompt cardiac evaluation.

**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 induction of mixed/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; such screening should include a detailed psychiatric history, including a family history of bipolar, manic disorder, and depression.

**Emergence of New 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 0.1% (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 and the postmarketing experience of some medications indicated for the treatment of ADHD. Although 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 ages 7 to 10 years who were randomized to either methylphenidate or non-medication treatment groups over 14 months, as well as in naturalistic subgroups of newly methylphenidate-treated and non-medication treated children over 36 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 on 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 this period of development. In a controlled trial of amphetamine (d to l enantiomer ratio of 3:1) in adolescents, mean weight change from baseline within the initial 4 weeks of therapy was -1.1 lbs. and -2.8 lbs., respectively, for patients receiving 10 mg and 20 mg of amphetamine (d to l enantiomer ratio of 3:1). Higher doses were associated with greater weight loss within the initial 4 weeks of treatment. In a controlled trial of lisdexamfetamine in children ages 6 to 12 years, mean weight loss from baseline after 4 weeks of therapy was -0.9, -1.9, and -2.5 lb, respectively, for patients receiving 30 mg, 50 mg, and 70 mg of lisdexamfetamine, compared to a 1 lb weight gain for patients receiving placebo. Higher doses were associated with greater weight loss with 4 weeks of treatment. Careful follow-up for weight in children ages 6 to 12 years who received lisdexamfetamine over 12 months suggests that consistently medicated children (i.e., treatment for 7 days per week throughout the year) have a slowing in growth rate measured by body weight as demonstrated by an age- and sex-normalized mean change from baseline in percentile of -13.4 over 1 year (average percentile at baseline and 12 months, were 60.6 and 47.2, respectively). 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 seizure, 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 Vyvanse feasible should be prescribed or dispensed at one time in order to minimize the possibility of overdose. Vyvanse should be used with caution in patients who use other sympathomimetic drugs.

**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.

**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.

Prescribers or other health professionals should inform patients, their families, and their caregivers about the benefits and risks associated with treatment with lisdexamfetamine and should counsel them in its appropriate use. A Patient Medication Guide is available for Vyvanse. The prescriber or health professional should instruct patients, their families, and their caregivers to read the Medication Guide and should assist them in understanding its contents. Patients should be given the opportunity to discuss the contents of the Medication Guide and to obtain answers to any questions they may have. The complete text of the Medication Guide is reprinted at the end of this document.

**Drug Interactions:**  
**Urinary acidifying agents**—These agents (ammonium chloride, sodium acid phosphate, etc.) increase the concentration of the ionized species of the amphetamine molecule, thereby increasing urinary excretion. Both groups of agents lower blood levels and efficacy of amphetamines.

**Adrenergic blockers**—Adrenergic blockers are inhibited by amphetamines.

**Antidepressants, tricyclic**—Amphetamines may enhance the activity of tricyclic antidepressants or sympathomimetic agents; d-amphetamine with desipramine or protriptyline and possibly other tricyclics cause striking and sustained increases in the concentration of d-amphetamine in the brain; cardiovascular effects can be potentiated.

**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 hypertensive crisis. A variety of toxic neurological effects and malignant hyperpyrexia can occur, sometimes with fatal results.

**Antihistamines**—Amphetamines may counteract the sedative effect of antihistamines.

**Antihypertensives**—Amphetamines may antagonize the hypotensive effects of antihypertensives.

**Chlorpromazine**—Chlorpromazine blocks dopamine and norepinephrine receptors, thus inhibiting the central stimulant effects of amphetamines and can be used to treat amphetamine poisoning.

**Ethosuximide**—Amphetamines may delay intestinal absorption of ethosuximide.

**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.

**Methanamine therapy**—Urinary excretion of amphetamines is increased, and efficacy is reduced by acidifying agents used in methanamine therapy.

**Norepinephrine**—Amphetamines enhance the adrenergic effect of norepinephrine.

**Phenobarbital**—Amphetamines may delay intestinal absorption of phenobarbital; co-administration of phenobarbital 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:** Carcinogenicity studies of lisdexamfetamine have not been performed. 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 30 mg/kg/day in male mice, 19 mg/kg/day in female mice, and 5 mg/kg/day in male and female rats. Lisdexamfetamine dimesylate was not clastogenic in the mouse bone marrow micronucleus test *in vivo* and was negative when tested in the *E. coli* and *S. typhimurium* components of the Ames test and in the L5178Y/TK<sup>+</sup> mouse lymphoma assay *in vitro*.

Amphetamine (d to l enantiomer 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.

**Pregnancy:** Pregnancy Category C. Reproduction studies of lisdexamfetamine have not been performed. Amphetamine (d to l enantiomer ratio of 3:1) had no apparent effects on embryofetal morphological development or survival when orally administered to pregnant rats and rabbits throughout the period of organogenesis at doses of up to 6 and 16 mg/kg/day, respectively. Fetal malformations and death have been reported in mice following parental administration of dextroamphetamine doses of 50 mg/kg/day or greater to pregnant animals. Administration of these doses was also associated with severe maternal toxicity. A number of studies in rodents indicate that prenatal 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 bone deformity, tracheo-esophageal fistula, and anal atresia (vater 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 amphetamine 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 lassitude.

**Use in Nursing Mothers:** Amphetamines are excreted in human milk. Mothers taking amphetamines should be advised to refrain from nursing.

**Pediatric Use:** Vyvanse is indicated for use in children aged 6 to 12 years. A study was conducted in which juvenile rats received oral doses of 4, 10, or 40 mg/kg/day of lisdexamfetamine from day 7 to day 63 of age. These doses are approximately 0.3, 0.7, and 3 times the maximum recommended human daily dose of 70 mg on a mg/m<sup>2</sup> basis. Dose-related decreases in food consumption, bodyweight gain, and crown-rump length were seen; after a four week drug-free recovery period, bodyweights and crown-rump lengths were significantly reduced in females but were still substantially reduced in males. Time to vaginal opening was delayed in females at the highest dose, but there were no drug effects on fertility when the animals were mated beginning on day 85 of age.

In a study in which juvenile dogs received lisdexamfetamine for 6 months beginning at 10 weeks of age, decreased bodyweight gain was seen at all doses tested (2, 5, and 12 mg/kg/day, which are approximately 0.5, 1, and 3 times the maximum recommended human daily dose on a mg/m<sup>2</sup> basis). This effect partially or fully reversed during a four week drug-free recovery period.

**Use in Children under Six Years of Age:** Lisdexamfetamine dimesylate has not been studied in 3-5 year olds. 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:** Vyvanse has not been studied in the geriatric population.

**ADVERSE EVENTS**  
The premarketing development program for Vyvanse included exposures in a total of 404 participants in clinical trials (348 pediatric patients and 56 healthy adult subjects). Of these, 348 pediatric patients (ages 6 to 12) were evaluated in two controlled clinical studies (one parallel-group and one crossover), one open-label extension study, and one single-dose clinical pharmacology study. The information included in this section is based on data from the 4-week parallel-group controlled clinical trial in pediatric patients with ADHD. 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, MedRA terminology has been used to classify reported 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:** Ten percent (21/218) of Vyvanse-treated patients discontinued due to adverse events compared to 1% (1/72) who received placebo. The most frequent adverse events leading to discontinuation and considered to be drug-related (i.e., leading to discontinuation in at least 1% of Vyvanse-treated patients and at a rate at least twice that of placebo) were ECG voltage criteria for ventricular hypertrophy, tic, vomiting, psychomotor hyperactivity, insomnia, and rash (2/218 each; 1%).

**Adverse events occurring in a controlled trial:** Adverse events reported in a 4-week clinical trial in pediatric patients treated with Vyvanse or placebo are presented in the table 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 investigators. 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 additional adverse reactions have been associated with the use of amphetamine, amphetamine (d to l enantiomer ratio of 3:1), or Vyvanse:

**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 at recommended doses, overstimulation, restlessness, dizziness, euphoria, dyskinesia, dysphoria, depression, tremor, headache, exacerbation of motor and phonic tics and Tourette's syndrome, seizures, stroke.

**Gastrointestinal:** Dryness of the mouth, unpleasant taste, diarrhea, constipation.

**Allergic:** Urticaria, hypersensitivity reactions including angioedema and anaphylaxis. Serious skin rashes, including Stevens Johnson Syndrome and toxic epidermal necrolysis have been reported.

**Endocrine:** Impotence, changes in libido.

**DRUG ABUSE AND DEPENDENCE**  
**Controlled Substance Class**  
Vyvanse is classified as a Schedule II controlled substance.

Amphetamines have been extensively abused. Tolerance, extreme psychological dependence, and severe social disability have occurred. There are reports of patients who have increased the dosage of amphetamine administration results 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.

**Human Studies**  
In a human abuse liability study, when equivalent oral doses of 100 mg lisdexamfetamine dimesylate and 40 mg immediate release d-amphetamine sulfate were administered to individuals with a history of drug abuse, lisdexamfetamine 100 mg produced subjective responses on a scale of "Drug Liking Effects" "Amphetamine Effects", and "Stimulant Effects" that were significantly less than d-amphetamine immediate release 40 mg. However, oral administration of 150 mg lisdexamfetamine produced increases in positive subjective responses on these scales that were statistically indistinguishable from the positive subjective responses produced by 40 mg oral immediate-release d-amphetamine and 200 mg of diethylpropion (C-IV).

Intravenous administration of 50 mg lisdexamfetamine to individuals with a history of drug abuse produced positive subjective responses on scales measuring "Drug Liking", "Euphoria", "Amphetamine Effects", and "Benzedrine Effects" that were greater than placebo but less than those produced by an equivalent dose (20 mg) of intravenous d-amphetamine.

**Animal Studies**  
In animal studies, lisdexamfetamine produced behavioral effects qualitatively similar to those of the CNS stimulant d-amphetamine. In monkeys trained to self-administer cocaine, intravenous lisdexamfetamine maintained self-administration at a rate that was statistically less than that for cocaine, but greater than that of placebo.

**OVERDOSAGE**  
Individual response to amphetamines varies widely. Toxic symptoms may occur idiosyncratically at low doses.

**Symptoms:** Manifestations of acute overdose with amphetamines include restlessness, tremor, hyperreflexia, rapid respiration, confusion, assaultiveness, hallucinations, panic states, hyperpyrexia and rhabdomyolysis. Fatigue and depression usually follow the central nervous system stimulation. Cardiovascular effects include arrhythmias, hypertension or hypotension and circulatory collapse. Gastrointestinal symptoms include nausea, vomiting, diarrhea, and abdominal cramps. Fatal poisoning is usually preceded by convulsions and

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. Acidification of the urine increases amphetamine excretion, but is believed to increase risk of acute renal failure if myoglobinuria is present. If acute severe hypertension complicates amphetamine overdose, administration of intravenous phentolamine 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 prolonged release of Vyvanse in the body should be considered when treating patients with overdose.

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