Vyvanse

Pharmacology, Warnings, Pregnancy, Lactation, Side Effects, IV Compatibility, Dosage, Additional Dosage

Pharmacology (Top)

Pharmacology

Lisdexamfetamine is a prodrug of dextroamphetamine. Dextroamphetamine is the dextro isomer of the d, l amphetamine compound. Amphetamines are non-catecholamine sympathomimetic amines with CNS stimulant activity. Peripheral actions include elevations in blood pressure and weak bronchodilator and respiratory stimulant activity.

Amphetamines are sympathetic amines that are known to stimulate the CNS by release of norepinephrine from central noradrenergic neurons. Higher levels of amphetamines may also cause dopamine to be released in the mesolimbic system. The d isomer of amphetamine is more potent than the l isomer in causing CNS excitatory effects and as an appetite suppressant. Peripheral effects of amphetamine-induced CNS stimulation include bronchodilation, respiratory stimulation, and AV and cardiac conduction enhancement. Clinical problems that have arisen as a result have included reflex bradycardia and other cardiac arrhythmias.

Lisdexamfetamine is approved by the FDA for the treatment of attention deficit/hyperactivity disorder.

Lisdexamfetamine is listed as a Schedule II drug under the Federal Controlled Substances Act of 1970.

Pharmacokinetics

There are no data on the bioavailability, plasma protein binding, volume of distribution, or plasma clearance for lisdexamfetamine.

The elimination half-life of lisdexamfetamine averages less than 1 hour in patients with normal renal and hepatic function.

Following oral administration, lisdexamfetamine is rapidly converted to dextroamphetamine and L-lysine by first pass hepatic or intestinal metabolism. Lisdexamfetamine is not metabolized by the CYP450 system. Approximately 96% of orally administered lisdexamfetamine is excreted in the urine and 0.3% in the feces. Approximately 42% of the lisdexamfetamine excreted in the urine is related to amphetamine, 25% to hippuric acid, and 2% is excreted as the parent compound.

Warnings (Top)

(Severity: General Warning Exists)

There are reports of extensive abuse with amphetamines. Tolerance, extreme psychological dependence and severe social disability have been reported, especially with prolonged therapy. Clinicians are advised to pay particular attention to individuals obtaining amphetamines for nontherapeutic use, distribution to others, or those who may increase the dose without first seeking medical advice. For these reasons and to decrease the possibility of an overdose, it is recommended that the smallest practical quantities be prescribed and that caution is employed patients who use other sympathomimetic drugs. Misuse of amphetamines may cause sudden death and serious cardiovascular adverse reactions.

Lisdexamfetamine is considered contraindicated for use in patients with advanced arteriosclerosis, symptomatic

cardiovascular disease, moderate to severe hypertension, hyperthyroidism, glaucoma, known hypersensitivity or idiosyncrasy to the sympathomimetic amines, a history of drug abuse, and those patients considered to be in an agitated state. Concomitant administration of lisdexamfetamine with, or within 14 days of discontinuing treatment with, a monoamine oxidase inhibitor (MAOI) is also considered contraindicated.

There are reports of sudden death associated with central nervous system (CNS) stimulant treatment administered at usual doses to pediatric and adolescent patients with structural cardiac abnormalities or other serious heart problems. In addition, there are reports of sudden death, stroke, and myocardial infarction in adults receiving normal doses of stimulant drugs. Therefore, the use of stimulant products is not recommended in any patient with known serious structural cardiac abnormalities, cardiomyopathy, serious heart rhythm abnormalities, coronary artery disease, or other serious cardiac problems that may place them at increased vulnerability to the sympathomimetic effects of a stimulant drug. Individuals being considered for treatment should undergo a physical examination to rule out the presence of cardiac disease and should undergo further cardiac assessment if such a condition is thought to be present. In addition a family medical history should be obtained, especially with regards to sudden death or ventricular arrhythmia. Patients who develop signs or symptoms of possible cardiac abnormalities during treatment with lisdexamfetamine should immediately undergo a complete cardiac evaluation.

Stimulant medications, including lisdexamfetamine, may cause a modest increase in average blood pressure and average heart rate. Some patients may experience larger increases in these parameters. Caution is recommended if the drug is to be prescribed to a patient with an underlying medical condition that might be compromised by increases in blood pressure or heart rate.

There are reports of exacerbation of symptoms of behavior disturbance and thought disorder associated with the use of stimulants, particularly in patients with preexisting psychotic disorder. Clinicians should be especially cautious in treating ADHD patients who have a known comorbid bipolar disorder due to possible induction of mixed/manic episode in such patients. It is recommended to screen all patients with comorbid depressive disorders for possible risk of bipolar disorder prior to initiating treatment with a stimulant. The assessment should include a detailed psychiatric history, as well as a family history, of suicide, bipolar disorder, and depression.

There are reports of treatment emergent psychotic or manic symptoms occurring in pediatric and adolescent patients without prior history of psychotic illness or mania. These events have been reported in patients receiving stimulants at usual doses. If these symptoms occur, clinicians should consider the possible causal role of the medication as well as possible discontinuation of treatment.

It is recommended to monitor patients for the appearance of, or worsening of, aggressive behavior or hostility.

Data are inadequate to determine whether chronic administration of amphetamines may be associated with growth inhibition; therefore, growth should be monitored during treatment with alterations in treatment enacted as necessary.

Stimulants, including lisdexamfetamine, may lower the seizure threshold irrespective of prior history of seizures and/or EEG abnormalities. It is recommended to discontinue treatment with lisdexamfetamine in patients who develop seizures.

There are reports of visual disturbances, particularly difficulties in accommodation and blurring of vision, associated with stimulant treatment.

Amphetamines have been reported to exacerbate motor and phonic tics and Tourette's syndrome. It is recommended to evaluate pediatric patients and their families for tics and Tourette's syndrome prior to initiation of therapy with lisdexamfetamine.

Lisdexamfetamine may impair the mental abilities necessary for potentially hazardous tasks such as driving or operating machinery.

Pregnancy (Top)

(Severity: Major Female Pregnancy Warning)

Lisdexamfetamine has been assigned to category C by the FDA. Animal studies have not been reported. There are no controlled data in human pregnancy. Lisdexamfetamine is only recommended for use during pregnancy when benefit outweighs risk.

Animal reproduction studies of lisdexamfetamine dimesylate have not been performed. Studies have been performed with the active metabolite of lisdexamfetamine, d-amphetamine, either alone or in combination with l-amphetamine.

Animal studies with dextroamphetamine have revealed evidence of embryotoxicity and teratogenicity. In addition, there has been one report of a case of severe congenital bony deformity, tracheoesophageal fistula, and anal atresia (vater association) in a baby born to a woman using dextroamphetamine with lovastatin during the first trimester of pregnancy.

Infants born to mothers dependent on amphetamines have an increased risk of premature delivery and low birth weight. These infants may experience symptoms of withdrawal including dysphoria, agitation, weakness, and exhaustion.

One study on the affects of methamphetamine abuse on pregnancy outcome reported that body weight, length, and head circumference were significantly decreased in neonates born to mothers who abused methamphetamines during pregnancy. The study also noted that the frequency of congenital anomalies was not significantly increased.

Lactation (Top)

(Severity: Major Lactation Warning)

Amphetamines are excreted into human milk. According to the manufacturer, breast-feeding is not recommended during administration of lisdexamfetamine.

Side Effects (Top)

General

All side effects listed, unless otherwise noted, were reported in pediatric patients.

Other 1

Other side effects have included decreased appetite (39%), headache, and pyrexia (2%).

Gastrointestinal

Gastrointestinal side effects have included upper abdominal pain (12%), dry mouth (5%), nausea (6%), and

vomiting (9%). Gastrointestinal side effects associated with amphetamine or lisdexamfetamine have included dryness of mouth, unpleasant taste, diarrhea, and constipation.

Metabolic

Metabolic side effects have included weight loss.

Nervous system

Nervous system side effects have included insomnia (19%), dizziness (5%), initial insomnia (4%), and somnolence (2%). Nervous system side effects associated with the use of recommended doses of amphetamine or lisdexamfetamine have included dyskinesia and seizures. Postmarketing reports have included psychotic episodes, mania, hallucination, and aggression.

Psychiatric

Psychiatric side effects have included irritability (10%), affect lability (3%), and tic (2%). Psychiatric side effects associated with the use of recommended doses of amphetamine or lisdexamfetamine have included overstimulation, restlessness, euphoria, dysphoria, depression, tremor, and exacerbation of motor and phonic tics and Tourette syndrome. Postmarketing reports have included dermatillomania.

Dermatologic

Dermatological side effects have included rash (3%). Dermatological side effects associated with amphetamine or lisdexamfetamine have included serious skin rashes, Stevens Johnson Syndrome, and toxic epidermal necrolysis.

Cardiovascular

Cardiovascular side effects associated with amphetamine or lisdexamfetamine have included palpitations, tachycardia, increased blood pressure, sudden death, stroke, and myocardial infarction. Cardiomyopathy has been associated with chronic amphetamine use.

Hypersensitivity

Hypersensitivity reactions associated with amphetamine or lisdexamfetamine have included urticaria, angioedema, anaphylaxis, Stevens Johnson Syndrome, and toxic epidermal necrolysis.

Genitourinary

Genitourinary side effects associated with amphetamine or lisdexamfetamine have included decreased libido (less than 2%), erectile dysfunction (less than 2%), impotence, and changes in libido.

Ocular

Ocular side effects including blurred vision have been reported.

IV Compatibility

Dosage (Top)

Usual Adult Dose

Attention Deficit Disorder

Initial dose: 30 mg orally once a day in the morning
If necessary, the initial daily dose may be increased by 10 mg to 20 mg approximately once a week up to a maximum daily dose of 70 mg

Usual Pediatric Dose

Attention Deficit Disorder

6 years or older:
Initial dose: 30 mg orally once a day in the morning
If necessary, the initial daily dose may be increased by 10 mg to 20 mg approximately once a week up to a maximum daily dose of 70 mg.

Lisdexamfetamine has not been studied in children under 6 years of age or adolescents. 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.

Additional Dosage (Top)

Renal Dose Adjustments

Data not available

Liver Dose Adjustments

Data not available

Dose Adjustments

The lowest effective dose should be prescribed.

Precautions

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serious heart problems. In addition, there are reports of sudden death, stroke, and myocardial infarction in adults receiving normal doses of stimulant drugs. Therefore, the use of stimulant products is not recommended in any patient with known serious structural cardiac abnormalities, cardiomyopathy, serious heart rhythm abnormalities, coronary artery disease, or other serious cardiac problems that may place them at increased vulnerability to the sympathomimetic effects of a stimulant drug. Individuals being considered for treatment should undergo a physical examination to rule out the presence of cardiac disease and should undergo further cardiac assessment if such a condition is thought to be present. In addition a family medical history should be obtained, especially with regards to sudden death or ventricular arrhythmia. Patients who develop signs or symptoms of possible cardiac abnormalities during treatment with lisdexamfetamine should immediately undergo a complete cardiac evaluation.

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Dialysis

Data not available

Other Comments

It is not recommended to administer lisdexamfetamine in the afternoon or evening due to an increased risk of insomnia.

Lisdexamfetamine capsules may be taken whole, or the capsule may be opened and the entire contents dissolved in a glass of water. The solution should be consumed immediately and should not be stored. The dose of a single capsule should not be divided. The contents of the entire capsule should be taken, and patients should not take anything less than one capsule per day.

Where possible, drug administration should be interrupted occasionally to determine if there is a recurrence of behavioral symptoms sufficient to require continued treatment.