HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use Vyvanse safely and effectively. See full prescribing information for Vyvanse.

Vyvanse® (lisdexamfetamine dimesylate) Capsules, CII

Initial U.S. Approval: 2007

WARNING: POTENTIAL FOR ABUSE
See full prescribing information for complete boxed warning

- Amphetamines have a high potential for abuse; prolonged administration may lead to dependence (9)
- Misuse of amphetamines may cause sudden death and serious cardiovascular adverse events

-----RECENT MAJOR CHANGES-----

Indications and Usage, Adolescents (1.1)	MM/YYYY
Dosage and Administration, Adolescents (2)	MM/YYYY
Warnings and Precautions, Long Term Suppression of Growth (5.6)	MM/YYYY

-----INDICATIONS AND USAGE-----

Vyvanse, a prodrug of the CNS stimulant dextroamphetamine, is indicated for the treatment of Attention Deficit Hyperactivity Disorder (ADHD). (1)

- Children: Efficacy was established in two trials in 6-12 year olds with ADHD. (14)
- Adolescents: Efficacy was established in one trial in 13-17 year olds with ADHD (14)
- Adults: Efficacy was established in two trials in adults with ADHD. (14)

-----DOSAGE AND ADMINISTRATION-----

- Recommended dose: Adults and pediatric patients ages (6-17); 30 mg once daily in the morning (2)
- Maximum dose: 70 mg once daily in the morning (2)

-----DOSAGE FORM AND STRENGTHS-----

- Capsules: 20 mg, 30 mg, 40 mg, 50 mg, 60 mg, 70 mg (3)

-----CONTRAINDICATIONS-----

- Advanced arteriosclerosis (4)
- Symptomatic cardiovascular disease (4)
- Moderate to severe hypertension (4)
- Hyperthyroidism (4)
- Known hypersensitivity or idiosyncrasy to sympathomimetic amines (4)
- Glaucoma (4)
- Agitated states (4)
- History of drug abuse (4)
- During or within 14 days following the administration of monoamine oxidase inhibitors (MAOI) (4, 7.3)

-----WARNINGS AND PRECAUTIONS-----

- Serious Cardiovascular Events: 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. Sudden death, stroke, and myocardial infarction have been reported in adults taking stimulant drugs at usual doses for ADHD. Stimulant products generally should not be used in patients with known structural cardiac abnormalities, cardiomyopathy, serious heart rhythm abnormalities, coronary artery disease, or other serious heart problems. (5.1)
- Increase in Blood Pressure: Monitor blood pressure and pulse at appropriate intervals in patients taking Vyvanse. Use with caution in patients for whom blood pressure increases may be problematic. (5.1)
- Psychiatric Adverse Events: Use of stimulants may cause treatment-emergent psychotic or manic symptoms in patients with no prior history, or exacerbation of symptoms in patients with pre-existing psychosis. Clinical evaluation for bipolar disorder is recommended prior to stimulant use. Monitor for aggressive behavior. (5.2)
- Seizures: may lower the convulsive threshold, and in the presence of seizures, should be discontinued. (5.3)
- Visual Disturbance: difficulties with accommodation and blurring of vision have been reported with stimulant treatment. (5.4)
- Tics: may exacerbate tics. Clinical evaluation for tics and Tourette's syndrome is recommended prior to stimulant administration. (5.5)
- Long-Term Suppression of Growth: monitor height and weight at appropriate intervals in pediatric patients taking Vyvanse. (5.6)

-----ADVERSE REACTIONS-----

- Children ages 6 to 12: Most common adverse reactions (incidence ≥5% and at a rate at least twice placebo) were decreased appetite, dizziness, dry mouth, irritability, insomnia, upper abdominal pain, nausea, vomiting, and decreased weight. (6.1)
- Adolescents ages 13 to 17: Most common adverse reactions (incidence ≥5% and at a rate at least twice placebo) were decreased appetite, insomnia, and decreased weight. (6.1)
- Adults: Most common adverse reactions (incidence ≥5% and at a rate at least twice placebo) were upper abdominal pain, diarrhea, nausea, fatigue, feeling jittery, irritability, anorexia, decreased appetite, headaches, anxiety, and insomnia. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Shire US Inc. at 1-800-828-2088 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch

-----DRUG INTERACTIONS-----

- Urinary acidifying agents may reduce blood levels of amphetamine. (7.2)
- Urinary alkalinizing agents may increase blood levels of amphetamine. (7.3)
- MAOI antidepressants are contraindicated. (4; 7.3)
- The effects of adrenergic blockers, antihistamines, antihypertensives, phenobarbital, and phenytoin may be reduced by amphetamines. (7.4)
- The effects of tricyclic antidepressants, meperidine, phenobarbital and phenytoin may be potentiated by amphetamines. (7.5)
- Norepinephrine may potentiate the effects of amphetamines. (7.7)

-----USE IN SPECIFIC POPULATIONS-----

- Pregnancy: Use only if the potential benefit justifies the potential risk to the fetus. Based on animal data, may cause fetal harm. (8.1)
- Nursing Mothers: should refrain from breastfeeding. (8.3)
- Pediatric Use: has not been studied in children under 6 years of age. (8.4)
- Geriatric Use: has not been studied in geriatric patients. (8.5)

See 17 for PATIENT COUNSELING INFORMATION and Medication Guide.

Revised: xx/xxxx

FULL PRESCRIBING INFORMATION: CONTENTS*

*Sections or subsections omitted from full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

WARNING: POTENTIAL FOR ABUSE

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 AMPHETAMINES MAY CAUSE SUDDEN DEATH AND SERIOUS CARDIOVASCULAR ADVERSE EVENTS.

1 INDICATIONS AND USAGE

1.1 Attention Deficit Hyperactivity Disorder

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, one controlled trial in adolescents aged 13 to 17, and two controlled trials in adults who met DSM-IV-TR® criteria for ADHD *[see CLINICAL STUDIES (14)]*.

A diagnosis of Attention Deficit Hyperactivity Disorder (ADHD; DSM-IV®) implies the presence of hyperactive-impulsive and/or inattentive symptoms that cause impairment and were present before the age of 7 years. The symptoms must cause clinically significant impairment, e.g. in social, academic, or occupational functioning, and be present in two or more settings, e.g. school (or work) and at home. The symptoms must not be better accounted for by another mental disorder. For the Inattentive Type, at least 6 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 6 of the following symptoms (or adult equivalent 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 patient and not solely on the presence of the required number of DSM-IV 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 patients with this syndrome. Stimulants are not intended for use in patients who exhibit symptoms secondary to environmental factors and/or other primary psychiatric disorders, including psychosis. Appropriate educational/vocational placement is essential and psychosocial intervention is often helpful. 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 patient's symptoms and on the level of functional impairment.

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.

2 DOSAGE AND ADMINISTRATION

Dosage should be individualized according to the therapeutic needs and response of the patient. Vyvanse should be administered at the lowest effective dosage.

In patients who are either starting treatment for the first time or switching from another medication, 30 mg once daily in the morning is the recommended dose. If the decision is made in the judgment of the clinician to increase the dose beyond 30 mg/day, daily dosage may be adjusted in increments of 10 mg or 20 mg at approximately weekly intervals. The maximum recommended dose is 70 mg/day; doses greater than 70 mg/day of Vyvanse have not been studied. Vyvanse has not been studied in children under 6 years of age.

Vyvanse should be taken in the morning. Afternoon doses should be avoided because of the potential for insomnia.

Vyvanse may be taken with or without food.

Vyvanse 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.

3 DOSAGE FORM AND STRENGTHS

Vyvanse capsules 20 mg: ivory body/ivory cap (imprinted with NRP104 or S489 and 20 mg)

Vyvanse capsules 30 mg: white body/orange cap (imprinted with NRP104 or S489 and 30 mg)

Vyvanse capsules 40 mg: white body/blue green cap (imprinted with NRP104 or S489 and 40 mg)

Vyvanse capsules 50 mg: white body/blue cap (imprinted with NRP104 or S489 and 50 mg)

Vyvanse capsules 60 mg: aqua blue body/aqua blue cap (imprinted with NRP104 or S489 and 60 mg)

Vyvanse capsules 70 mg: blue body/orange cap (imprinted with NRP104 or S489 and 70 mg)

4 CONTRAINDICATIONS

- Advanced arteriosclerosis, symptomatic cardiovascular disease, moderate to severe hypertension, hyperthyroidism, known hypersensitivity or idiosyncratic reaction to 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 crises may result) *[See Drug Interactions (7.3)]*

5 WARNINGS AND PRECAUTIONS

5.1 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, or other serious cardiac problems that may place them at increased vulnerability to the sympathomimetic effects of a stimulant drug *[see CONTRAINDICATIONS (4)]*.

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 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 problems. Adults with such abnormalities should also generally not be treated with stimulant drugs *[see CONTRAINDICATIONS (4)]*.

Hypertension and Other Cardiovascular Conditions

Stimulant medications cause a modest increase in average blood pressure (about 2-4 mm Hg) 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 (4)]*.

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 exertional chest pain, unexplained syncope, or other symptoms suggestive of cardiac disease during stimulant treatment should undergo a prompt cardiac evaluation.

5.2 Psychiatric Adverse Events

Pre-existing Psychosis

Administration of stimulants may exacerbate symptoms of behavior disturbance and thought disorder in patients with a pre-existing psychotic disorder.

Bipolar Illness

Particular care should be taken in using stimulants to treat ADHD in patients with comorbid bipolar disorder because of concern for possible induction of a 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 suicide, bipolar 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 a 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 of ADHD should be monitored for the appearance of, or worsening of, aggressive behavior or hostility.

5.3 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.

5.4 Visual Disturbance

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

5.5 Tics

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

5.6 Long-Term Suppression of Growth

In a controlled trial of Vyvanse 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 lbs., respectively, for patients receiving 30 mg, 50 mg, and 70 mg of Vyvanse, 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 Vyvanse 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 percentiles at baseline and 12 months were 60.6 and 47.2, respectively). In a 4-week controlled trial of Vyvanse in adolescents ages 13 to 17 years, mean weight loss from baseline to endpoint was -2.7, -4.3, and -4.8 lbs., respectively, for patients receiving 30 mg, 50 mg, and 70 mg of Vyvanse, compared to a 2.0 lb weight gain for patients receiving placebo.

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. Higher doses were associated with greater weight loss within the initial 4 weeks of treatment.

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.

5.7 Prescribing and Dispensing

The least amount of amphetamine feasible should be prescribed or dispensed at one time in order to minimize the possibility of overdosage. Vyvanse should be used with caution in patients who use other sympathomimetic drugs.

6 ADVERSE REACTIONS

6.1 Clinical Studies Experience

The premarketing development program for Vyvanse included exposures in a total of 995 participants in clinical trials (348 pediatric patients aged 6 to 12 years, 233 adolescent patients aged 13 to 17 years, 358 adult patients and 56 healthy adult subjects). Of these, 348 pediatric (aged 6 to 12) patients 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, 233 adolescent (aged 13 to 17) patients were evaluated in one controlled clinical study, and 358 adult patients were evaluated in one controlled clinical study and one open-label extension study. The information included in this section is based on data from the 4-week parallel-group controlled clinical studies in pediatric and adult patients with ADHD. Adverse reactions were assessed by collecting adverse events, results of physical examinations, vital signs, weights, laboratory analyses, and ECGs.

Adverse reactions 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 reactions without first grouping similar types of reactions into a smaller number of standardized reactions categories. In the tables and listings that follow, MedDRA terminology has been used to classify reported adverse reactions.

The stated frequencies of adverse reactions represent the proportion of individuals who experienced a treatment-emergent adverse reaction of the type listed at least once.

<u>Adverse Reactions Associated with Discontinuation of Treatment in Clinical Trials</u>

In the controlled pediatric (aged 6 to 12) trial, 9% (20/218) of Vyvanse-treated patients discontinued due to adverse reactions 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%).

In the controlled adolescent (aged 13 to 17) trial, 4% (10/233) of Vyvanse-treated patients discontinued due to adverse events compared to 1% (1/77) who received placebo. The most frequent adverse reactions leading to

discontinuation and considered to be drug-related were irritability (3/233; 1%), decreased appetite (2/233; 1%), and insomnia (2/233; 1%).

In the controlled adult trial, 6% (21/358) of Vyvanse-treated patients discontinued due to adverse events compared to 2% (1/62) 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 insomnia (8/358; 2%), tachycardia (3/358; 1%), irritability (2/358; 1%), hypertension (4/358; 1%), headache (2/358; 1%), anxiety (2/358; 1%), and dyspnea (3/358; 1%).

Adverse Reactions Occurring at an Incidence of 2% or More Among Vyvanse Treated Patients in Clinical Trials

Adverse reactions reported in the controlled trials in pediatric (aged 6 to 17 years) and adult patients treated with Vyvanse or placebo are presented in Tables 1, 2, and 3 below. The prescriber should be aware that these figures cannot be used to predict the incidence of adverse reactions 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 treatment 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 reaction incidence rate in the population studied.

Pediatric

Table 1 Adverse Reactions Reported by 2% or More of Children (Aged 6 to 12 Years) Taking Vyvanse in a 4-Week Clinical Trial

Body System	Preferred Term	Vyvanse (n=218)	Placebo (n=72)
Gastrointestinal Disorders	Abdominal Pain Upper	12%	6%
	Vomiting	9%	4%
	Nausea	6%	3%
	Dry Mouth	5%	0%
General Disorder and Administration Site Conditions	Pyrexia	2%	1%
Investigations	Weight Decreased	9%	1%
Metabolism and Nutrition	Decreased Appetite	39%	4%
Nervous System Disorders	Dizziness	5%	0%
	Somnolence	2%	1%
Psychiatric Disorders	Insomnia[a]	23%	3%
	Irritability	10%	0%
	Affect lability	3%	0%
	Tic	2%	0%
Skin and Subcutaneous Tissue Disorders	Rash	3%	0%

[a] Insomnia includes the following preferred terms reported in the study: Initial Insomnia, Insomnia.

Note: This table includes those reactions for which the incidence in patients taking Vyvanse is at least twice the incidence in patients taking placebo.

Table 2 Adverse Reactions Reported by 2% or More of Adolescent (Aged 13 to 17 Years) Patients Taking Vyvanse in a 4-Week Clinical Trial

Body System	Preferred Term	Vyvanse (n=233)	Placebo (n=77)
Gastrointestinal Disorders	Dry Mouth	4%	1%
Investigations	Weight Decreased	9%	0%
Metabolism and Nutrition	Decreased Appetite	34%	3%
Psychiatric Disorders	Insomnia[b]	13%	4%

[b] Insomnia includes the following preferred terms reported in the study: Initial Insomnia, Insomnia.

Note: This table includes those reactions for which the incidence in patients taking Vyvanse is at least twice the incidence in patients taking placebo.

Adult

Table 3 Adverse Reactions Reported by 2% or More of Adult Patients Taking Vyvanse in a 4-Week Clinical Trial

Body System	Preferred Term	Vyvanse (n=358)	Placebo (n=62)
Gastrointestinal Disorders	Dry Mouth	26%	3%
	Diarrhea	7%	0%
	Nausea	7%	0%
General Disorder and Administration Site Conditions	Feeling Jittery	4%	0%
Investigations	Blood Pressure Increased	3%	0%
	Heart Rate Increased	2%	0%
Metabolism and Nutrition Disorders	Decreased Appetite	27%	3%
	Anorexia	5%	0%
Nervous System Disorders	Tremor	2%	0%
Psychiatric Disorders	Insomnia[c]	27%	8%
	Anxiety	6%	0%
	Agitation	3%	0%
	Restlessness	3%	0%
Respiratory ,Thoracic, and Mediastinal Disorders	Dyspnea	2%	0%
Skin and Subcutaneous Tissue Disorders	Hyperhidrosis	3%	0%

[c] Insomnia includes the following preferred terms reported in the study: Initial Insomnia, Insomnia, Middle Insomnia.

Note: This table includes those events for which the incidence in patients taking Vyvanse is at least twice the incidence in patients taking placebo.

In addition, adverse reactions observed at a rate of less than 2% included decreased libido and erectile dysfunction.

Vital Signs

Weight Loss – In the controlled adult trial, mean weight loss after 4 weeks of therapy was 2.8 lbs, 3.1 lbs, and 4.3 lbs, for patients receiving final doses of 30 mg, 50 mg, and 70 mg of Vyvanse, respectively, compared to a mean weight gain of 0.5 lbs for patients receiving placebo.

6.2 Postmarketing Reports

The following adverse reactions have been identified during post approval use of Vyvanse. Because these reactions are reported voluntarily from a population of uncertain size, it is not possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Cardiac Disorders - Palpitation

Eye Disorders - Vision blurred, mydriasis, diplopia

General Disorders and Administration Site Conditions - Fatigue

Hepatobiliary Disorders - Eosinophilic Hepatitis

Immune System Disorders – Anaphylactic reaction, hypersensitivity

Nervous System Disorders – Somnolence**,** seizure, dyskinesia

Psychiatric Disorder - Psychotic episodes, mania, hallucination, depression, aggression, dysphoria, euphoria, logorrhea

Skin and Subcutaneous Tissue Disorder - Stevens-Johnson Syndrome, angioedema, urticaria

6.3 Adverse Reactions Associated with the Use of Amphetamine

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, insomnia, 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, other gastrointestinal disturbances.

Allergic

Urticaria, rashes, and hypersensitivity reactions, including angioedema and anaphylaxis. Serious skin reactions, including Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis have been reported.

Endocrine

Impotence, changes in libido.

7 DRUG INTERACTIONS

7.1 Agents Whose Blood Levels May be Impacted by Vyvanse

Extended release guanfacine: In a drug interaction study (N=40), administration of an extended release guanfacine (4 mg) in combination with Vyvanse (50mg) increased guanfacine maximum plasma concentration by 19%, whereas, exposure (area under the curve; AUC) was increased by 7%. These small changes are not expected to be clinically meaningful. In this study, no effect on d-amphetamine exposure was observed following co-administration of extended release guanfacine and Vyvanse.

7.2 Agents that Lower Blood Levels of Amphetamines

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.

Methenamine Therapy
Urinary excretion of amphetamines is increased, and efficacy is reduced, by acidifying agents used in methenamine therapy.

7.3 Agents that Increase Blood Levels of Amphetamines

Urinary Alkalinizing Agents
These agents (acetazolamide, some thiazides) increase the concentration of the non-ionized species of the amphetamine molecule, thereby decreasing urinary excretion.

Monoamine Oxidase Inhibitors
MAOI antidepressants, 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.

7.4 Agents Whose Effects May be Reduced by Amphetamines

Adrenergic Blockers
Adrenergic blockers are inhibited by amphetamines.

Antihistamines
Amphetamines may counteract the sedative effect of antihistamines.

Antihypertensives
Amphetamines may antagonize the hypotensive effects of antihypertensives.

Veratrum Alkaloids
Amphetamines inhibit the hypotensive effect of veratrum alkaloids.

Ethosuximide
Amphetamines may delay intestinal absorption of ethosuximide.

7.5 Agents Whose Effects May be Potentiated 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.

Meperidine
Amphetamines potentiate the analgesic effect of meperidine.

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.

7.6 Agents that May Reduce the Effects of Amphetamines

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

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.

7.7 Agents that May Potentiate the Effects of Amphetamines

Norepinephrine
Amphetamines enhance the adrenergic effect of norepinephrine.

Propoxyphene Overdosage
In cases of propoxyphene overdosage, amphetamine CNS stimulation is potentiated and fatal convulsions can occur.

7.8 Drug/Laboratory Test Interactions

Amphetamines can cause a significant elevation in plasma corticosteroid levels. This increase is greatest in the evening. Amphetamine may interfere with urinary steroid determinations.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

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, as noted below.

Teratogenic Effects

Pregnancy Category C

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 parenteral administration of d-amphetamine 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 longterm 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 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 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 lassitude.

8.2 Labor and Delivery

The effects of Vyvanse on labor and delivery in humans is unknown.

8.3 Nursing Mothers

Amphetamines are excreted into human milk. Mothers taking amphetamines should be advised to refrain from nursing.

8.4 Pediatric Use

Vyvanse is indicated for use in pediatric patients with ADHD aged 6 to 17 years. Vyvanse has not been studied in children under 6 years of age. Long-term effects of amphetamines in children have not been well established.

A study was conducted in which juvenile rats received oral doses of 4, 10, or 40 mg/kg/day of lisdexamfetamine dimesylate 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^2 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 had significantly recovered 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 dimesylate 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^2 basis). This effect partially or fully reversed during a four-week drug-free recovery period.

8.5 Geriatric Use

Vyvanse has not been studied in the geriatric population.

9 DRUG ABUSE AND DEPENDENCE

9.1 Controlled Substance

Vyvanse is classified as a Schedule II controlled substance.

9.2 Abuse and Dependence

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 to levels many times higher than recommended. Abrupt cessation following prolonged high-dosage 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 dimesylate 100 mg produced subjective responses on a scale of “Drug Liking Effects” (primary endpoint) that were significantly less than d-amphetamine immediate-release 40 mg. However, oral administration of 150 mg lisdexamfetamine dimesylate produced increases in positive subjective responses on this scale that were statistically indistinguishable from the positive subjective responses produced by 40 mg of oral immediate-release d-amphetamine and 200 mg of diethylpropion (C-IV).[1]

Intravenous administration of 50 mg lisdexamfetamine dimesylate 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 dimesylate produced behavioral effects qualitatively similar to those of the CNS stimulant d-amphetamine. In monkeys trained to self-administer cocaine, intravenous lisdexamfetamine dimesylate maintained self-administration at a rate that was statistically less than that for cocaine, but greater than that of placebo.

10 OVERDOSAGE

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

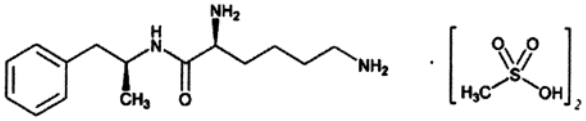
Symptoms: Manifestations of acute overdosage with amphetamines include restlessness, tremor, hyperreflexia, rapid respiration, confusion, assaultiveness, hallucinations, panic states, hyperpyrexia, and rhabdomyolysis. Fatigue and depression usually follow the central nervous system stimulation. Cardiovascular 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 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. 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 overdosage, 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.

11 DESCRIPTION

Vyvanse (lisdexamfetamine dimesylate) is designed as a capsule for once-a-day oral administration. The chemical designation for lisdexamfetamine dimesylate is (2*S*)-2,6-diamino-*N*-[(1*S*)-1-methyl-2-phenylethyl] hexanamide dimethanesulfonate. The molecular formula is $C_{15}H_{25}N_3O•(CH_4O_3S)_2$, which corresponds to a molecular weight of 455.60. The chemical structure is:



Lisdexamfetamine dimesylate is a white to off-white powder that is soluble in water (792 mg/mL). Vyvanse capsules contain 20 mg, 30 mg, 40 mg, 50 mg, 60 mg, and 70 mg of lisdexamfetamine dimesylate and the following inactive ingredients: microcrystalline cellulose, croscarmellose sodium, and magnesium stearate. The capsule shells contain gelatin, titanium dioxide, and one or more of the following: D&C Red #28, D&C Yellow #10, FD&C Blue #1, FD&C Green #3, and FD&C Red #40.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Lisdexamfetamine is a prodrug of dextroamphetamine. After oral administration, lisdexamfetamine is rapidly absorbed from the gastrointestinal tract and converted to dextroamphetamine, which is responsible for the drug's activity. Amphetamines are non-catecholamine sympathomimetic amines with CNS stimulant activity. The mode of therapeutic action in Attention Deficit Hyperactivity Disorder (ADHD) is not known. Amphetamines are thought to block the reuptake of norepinephrine and dopamine into the presynaptic neuron and increase the release of these monoamines into the extraneuronal space. The parent drug, lisdexamfetamine, does not bind to the sites responsible for the reuptake of norepinephrine and dopamine *in vitro*.

12.3 Pharmacokinetics

Pharmacokinetic studies of dextroamphetamine after oral administration of lisdexamfetamine have been conducted in healthy adult and pediatric (aged 6 to 12) patients with ADHD.

In 18 pediatric patients (aged 6 to 12) with ADHD, the T_{max} of dextroamphetamine was approximately 3.5 hours following single-dose oral administration of lisdexamfetamine dimesylate either 30 mg, 50 mg, or 70 mg after an 8-hour overnight fast. The T_{max} of lisdexamfetamine was approximately 1 hour. Linear pharmacokinetics of dextroamphetamine after single-dose oral administration of lisdexamfetamine dimesylate was established over the dose range of 30 mg to 70 mg in children aged 6 to 12 years.

There is no unexpected accumulation of dextroamphetamine AUC at steady state in healthy adults and no accumulation of lisdexamfetamine after once-daily dosing for 7 consecutive days.

Food does not affect the observed AUC and C_{max} of dextroamphetamine in healthy adults after single-dose oral administration of 70 mg of Vyvanse capsules but prolongs T_{max} by approximately 1 hour (from 3.8 hrs at fasted state to 4.7 hrs after a high fat meal). After an 8-hour fast, the AUCs for dextroamphetamine following oral administration of lisdexamfetamine dimesylate in solution and as intact capsules were equivalent.

Weight/Dose normalized AUC and C_{max} were 22% and 12% lower, respectively, in adult females than in males on day 7 following a 70 mg/day dose of lisdexamfetamine dimesylate for 7 days. Weight/Dose normalized AUC and C_{max} values were the same in girls and boys following single doses of 30-70 mg.

Metabolism and Excretion

After oral administration, lisdexamfetamine is rapidly absorbed from the gastrointestinal tract. Lisdexamfetamine is converted to dextroamphetamine and l-lysine, which is believed to occur by first-pass intestinal and/or hepatic metabolism. Lisdexamfetamine is not metabolized by cytochrome P450 enzymes. Following the oral administration of a 70 mg dose of radiolabeled lisdexamfetamine dimesylate to 6 healthy subjects, approximately 96% of the oral dose radioactivity was recovered in the urine and only 0.3% recovered in the feces over a period of 120 hours. Of the radioactivity recovered in the urine, 42% of the dose was related to amphetamine, 25% to hippuric acid, and 2% to intact lisdexamfetamine. Plasma concentrations of unconverted lisdexamfetamine are low and transient, generally becoming non-quantifiable by 8 hours after administration. The plasma elimination half-life of lisdexamfetamine typically averaged less than one hour in studies of lisdexamfetamine dimesylate in volunteers.

Dextroamphetamine is known to inhibit monoamine oxidase. The ability of dextroamphetamine and its metabolites to inhibit various P450 isozymes and other enzymes has not been adequately elucidated. *In vitro* experiments with human microsomes indicate minor inhibition of CYP2D6 by amphetamine and minor inhibition of CYP1A2, 2D6, and 3A4 by one or more metabolites, but there are no *in vivo* studies of p450 enzyme inhibition.

Special Populations

Age

The pharmacokinetics of dextroamphetamine is similar in pediatric (aged 6 to 12) and adolescent (aged 13 to 17) ADHD patients, and healthy adult volunteers. Any differences in kinetics seen after oral administration are a result of differences in mg/kg dosing.

Gender

Systemic exposure to dextroamphetamine is similar for men and women given the same mg/kg dose.

Race

Formal pharmacokinetic studies for race have not been conducted.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis/ Mutagenesis and Impairment of Fertility

Carcinogenicity studies of lisdexamfetamine dimesylate 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^{+-} 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.

13.2 Animal Toxicology

Acute administration of high doses of amphetamine (d- or d,l-) has been shown to produce long-lasting neurotoxic effects, including irreversible nerve fiber damage, in rodents. The significance of these findings to humans is unknown.

14 CLINICAL STUDIES

The efficacy of Vyvanse in the treatment of ADHD was established on the basis of two controlled trials in children aged 6 to 12 years, one controlled trial in adolescents aged 13 to 17 years, and two controlled trials in adults who met Diagnostic and Statistical Manual of Mental Disorders, 4th edition (DSM-IV-TR) criteria for ADHD *[see INDICATIONS AND USAGE (1)]*.

Pediatric

A double-blind, randomized, placebo-controlled, parallel-group study was conducted in children aged 6 to 12 (N=290) who met DSM-IV criteria for ADHD (either the combined type or the hyperactive-impulsive type). Patients were randomized to receive final doses of 30 mg, 50 mg, or 70 mg of Vyvanse or placebo once daily in the morning for a total of four weeks of treatment. All subjects receiving Vyvanse were initiated on 30 mg for the first week of treatment. Subjects assigned to the 50 mg and 70 mg dose groups were titrated by 20 mg per week until they achieved their assigned dose. The primary efficacy outcome was change in Total Score from baseline to endpoint in investigator ratings on the ADHD Rating Scale (ADHD-RS), a measure of the core symptoms of ADHD. Endpoint was defined as the last post-randomization treatment week (i.e. Weeks 1 through 4) for which a valid score was obtained. All Vyvanse dose groups were superior to placebo in the primary efficacy outcome. Mean effects at all doses were fairly similar, although the highest dose (70 mg/day) was numerically superior to both lower doses (30 mg/day and 50 mg/day). The effects were maintained throughout the day based on parent ratings (Conners' Parent Rating Scale) in the morning (approximately 10 am), afternoon (approximately 2 pm), and early evening (approximately 6 pm).

A double-blind, placebo-controlled, randomized, crossover design, analog classroom study was conducted in children aged 6 to 12 (N=52) who met DSM-IV criteria for ADHD (either the combined type or the hyperactive-impulsive type). Following a 3-week open-label dose titration with Adderall XR®, patients were randomly assigned to continue the same dose of Adderall XR (10 mg, 20 mg, or 30 mg), Vyvanse (30 mg, 50 mg, or 70 mg), or placebo once daily in the morning for 1 week each treatment. A significant difference in patient behavior, based upon the average of investigator ratings on the Swanson, Kotkin, Agler, M.Flynn, and Pelham (SKAMP)-Deportment scores across 7 assessments conducted at 2, 3, 4.5, 6, 8, 10, and 12 hours post-dose were observed between patients who received Vyvanse compared to patients who received placebo. The drug effect was similar for all 7 sessions.

A second double-blind, placebo-controlled, randomized, crossover design, analog classroom study was conducted in children aged 6 to 12 (N=129) who met DSM-IV criteria for ADHD (either the combined type or the hyperactive-impulsive type). Following a 4-week open-label dose titration with Vyvanse (30 mg, 50 mg, 70 mg), patients were randomly assigned to continue Vyvanse or placebo once daily in the morning for 1 week each treatment. A significant difference in patient behavior, based upon the average of investigator ratings on the SKAMP-Deportment scores across all 7 assessments conducted at 1.5, 2.5, 5.0, 7.5, 10.0, 12.0, and 13.0 hours post-dose, were observed between patients who received Vyvanse compared to patients who received placebo.

A double-blind, randomized, placebo-controlled, parallel-group study was conducted in adolescents aged 13 to 17 (N=314) who met DSM-IV criteria for ADHD. In this study, patients were randomized in a 1:1:1:1 ratio to a daily morning dose of Vyvanse (30 mg/day, 50 mg/day or 70 mg/day) or placebo for a total of four weeks of

treatment. All subjects receiving Vyvanse were initiated on 30 mg for the first week of treatment. Subjects assigned to the 50 mg and 70 mg dose groups were titrated by 20 mg per week until they achieved their assigned dose. The primary efficacy outcome was change in Total Score from baseline to endpoint in investigator ratings on the ADHD Rating Scale (ADHD-RS), a measure of the core symptoms of ADHD. Endpoint was defined as the last post-randomization treatment week (i.e. Weeks 1 through 4) for which a valid score was obtained. All Vyvanse dose groups were superior to placebo in the primary efficacy outcome.

Adult

A double-blind, randomized, placebo-controlled, parallel-group study was conducted in adults (N=420) who met DSM-IV criteria for ADHD. In this study, patients were randomized to receive final doses of 30 mg, 50 mg, or 70 mg of Vyvanse or placebo for a total of four weeks of treatment. All subjects receiving Vyvanse were initiated on 30 mg for the first week of treatment. Subjects assigned to the 50 mg and 70 mg dose groups were titrated by 20 mg per week until they achieved their assigned dose. The primary efficacy outcome was change in Total Score from baseline to endpoint in investigator ratings on the ADHD Rating Scale (ADHD-RS), a measure of the core symptoms of ADHD. Endpoint was defined as the last post-randomization treatment week (i.e. Weeks 1 through 4) for which a valid score was obtained. All Vyvanse dose groups were superior to placebo in the primary efficacy outcome.

The second study was a multi-center, randomized, double-blind, placebo-controlled, crossover design, modified analog classroom study of Vyvanse to simulate a workplace environment in 142 adults who met DSM-IV-TR criteria for ADHD. There was a 4-week open-label, dose optimization phase with Vyvanse (30 mg/day, 50 mg/day, or 70 mg/day in the morning). Subjects were then randomized to one of two treatment sequences: 1) Vyvanse (optimized dose) followed by placebo, each for one week, or 2) placebo followed by Vyvanse, each for one week. Efficacy assessments occurred at the end of each week, using the Permanent Product Measure of Performance (PERMP). The PERMP is a skill-adjusted math test that measures attention in ADHD. Vyvanse treatment, compared to placebo, resulted in a statistically significant improvement in attention across all post-dose time points, as measured by average PERMP total scores over the course of one assessment day, as well as at each time point measured. The PERMP assessments were administered at pre-dose (-0.5 hours) and at 2, 4, 8, 10, 12, and 14 hours post-dose.

15 REFERENCES

[1] Jasinski DR, Krishnan S. Abuse liability and safety of oral lisdexamfetamine dimesylate in individuals with a history of stimulant abuse. *Journal of Psychopharmacology.* 2009; 23(4);419-27.

16 HOW SUPPLIED/STORAGE AND HANDLING

Vyvanse capsules 20 mg: ivory body/ivory cap (imprinted with NRP104 or S489 and 20 mg), bottles of 100, NDC 59417-102-10

Vyvanse capsules 30 mg: white body/orange cap (imprinted with NRP104 or S489 and 30 mg), bottles of 100, NDC 59417-103-10

Vyvanse capsules 40 mg: white body/blue green cap (imprinted with NRP104 or S489 and 40 mg), bottles of 100, NDC 59417-104-10

Vyvanse capsules 50 mg: white body/blue cap (imprinted with NRP104 or S489 and 50 mg), bottles of 100, NDC 59417-105-10

Vyvanse capsules 60 mg: aqua blue body/aqua blue cap (imprinted with NRP104 or S489 and 60 mg), bottles of 100, NDC 59417-106-10

Vyvanse capsules 70 mg: blue body/orange cap (imprinted with NRP104 or S489 and 70 mg), bottles of 100, NDC 59417-107-10

Dispense in a tight, light-resistant container as defined in the USP.

Store at 25º C (77º F). Excursions permitted to 15-30º C (59-86º F) [see USP Controlled Room Temperature]

17 PATIENT COUNSELING INFORMATION

See Medication Guide

17.1 Information on Medication Guide

Prescribers or other health professionals should inform patients, their families, and their caregivers about the benefits and risks associated with treatment with Vyvanse 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 attached to the package insert.

17.2 Controlled Substance Status/Potential for Abuse, Misuse, and Dependence

Patients should be advised that Vyvanse is a federally controlled substance because it can be abused or lead to dependence. Additionally, it should be emphasized that Vyvanse should be stored in a safe place to prevent misuse and/or abuse. Patient history (including family history) of abuse or dependence on alcohol, prescription medicines, or illicit drugs should be evaluated *[See Drug Abuse and Dependence (9)]*.

17.3 Serious Cardiovascular Risks

Patients should be advised of serious cardiovascular risk (including sudden death, myocardial infarction, stroke, and hypertension) with Vyvanse. Patients who develop symptoms such as exertional chest pain, unexplained syncope, or other symptoms suggestive of cardiac disease during treatment should undergo a prompt cardiac evaluation [*See Warning and Precautions* (5.1)].

17.4 Psychiatric Risks

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 suicide, bipolar disorder, and/or depression. Additionally, stimulant therapy at usual doses may cause treatment-emergent psychotic or manic symptoms in patients without prior history of psychotic symptoms or mania [*See Warnings and Precautions* (5.2)].

17.5 Growth

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. [*See Warnings and Precautions* (5.6)].

17.6 Pregnancy

Patients should be advised to notify their physicians if they become pregnant or intend to become pregnant during treatment [*see Dosage and Administration (2) and Use in Specific Populations* (8.1)].

17.7 Nursing

Patients should be advised not to breast feed if they are taking Vyvanse *[see Use in Specific Populations (8.3)].*

17.8 Impairment in Ability to Operate Machinery or Vehicles

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.

Pharmacist: Medication Guide to be dispensed to patients

Manufactured for: Shire US Inc., Wayne, PA 19087

Made in USA

For more information call 1-800-828-2088

Vyvanse® is a trademark of Shire LLC

US Pat No. 7,105,486 and US Pat No. 7,223,735

Last Modified: xx/xxxx