LISDEXAMFETAMINE DIMESYLATE- lisdexamfetamine dimesylate capsules capsule
Solco Healthcare US,LLC

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use LISDEXAMFETAMINE DIMESYLATE CAPSULES safely and effectively. See full prescribing information for LISDEXAMFETAMINE DIMESYLATE CAPSULES.
LISDEXAMFETAMINE DIMESYLATE capsules, for oral use, CII
Initial U.S. Approval: 2007

WARNING: ABUSE AND DEPENDENCE

See full prescribing information for complete boxed warning.

- **CNS stimulants, including lisdexamfetamine dimesylate, other amphetamine-containing products, and methylphenidate, have a high potential for abuse and dependence (5.1, 9.3)**
- **Assess the risk of abuse prior to prescribing and monitor for signs of abuse and dependence while on therapy (5.1, 9.2)**

RECENT MAJOR CHANGES

Indications and Usage (1) 7/2021
Warnings and Precautions (5.5) 7/2021

INDICATIONS AND USAGE

Lisdexamfetamine dimesylate capsule is a central nervous system (CNS) stimulant indicated for the treatment of (1):

- Attention Deficit Hyperactivity Disorder (ADHD) in adults and pediatric patients 6 years and older
- Moderate to severe binge eating disorder (BED) in adults

Limitations of Use:

- Pediatric patients with ADHD younger than 6 years of age experienced more long-term weight loss than patients 6 years and older (8.4)
- Lisdexamfetamine dimesylate capsules are not indicated for weight loss. Use of other sympathomimetic drugs for weight loss has been associated with serious cardiovascular adverse events. The safety and effectiveness of lisdexamfetamine dimesylate capsule for the treatment of obesity have not been established (5.2)

DOSAGE AND ADMINISTRATION

Indicated Population	Initial Dose	Titration Schedule	Recommended Dose	Maximum Dose
ADHD (Adults and pediatric patients 6 years and older) (2.2)	30 mg every morning	10 mg or 20 mg weekly	30 mg to 70 mg per day	70 mg per day
BED (Adults) (2.3)	30 mg every morning	20 mg weekly	50 mg to 70 mg per day	70 mg per day

- Prior to treatment, assess for presence of cardiac disease (2.4)
- Severe renal impairment: Maximum dose is 50 mg/day (2.5)

- End stage renal disease (ESRD): Maximum dose is 30 mg/day (2.5)

DOSAGE FORMS AND STRENGTHS

- Capsules: 10 mg, 20 mg, 30 mg, 40 mg, 50 mg, 60 mg, 70 mg (3)

CONTRAINDICATIONS

- Known hypersensitivity to amphetamine products or other ingredients in lisdexamfetamine dimesylate capsule (4)
- Use with monoamine oxidase (MAO) inhibitor, or within 14 days of the last MAO inhibitor dose (4, 7.2)

WARNINGS AND PRECAUTIONS

- *Serious Cardiovascular Reactions:* Sudden death has been reported in association with CNS stimulant treatment at recommended doses in pediatric patients with structural cardiac abnormalities or other serious heart problems. In adults, sudden death, stroke, and myocardial infarction have been reported. Avoid use in patients with known structural cardiac abnormalities, cardiomyopathy, serious heart arrhythmia, or coronary artery disease (5.2)
- *Blood Pressure and Heart Rate Increases:* Monitor blood pressure and pulse. Consider benefits and risks before use in patients for whom blood pressure increases may be problematic (5.3)
- *Psychiatric Adverse Reactions:* May cause psychotic or manic symptoms in patients with no prior history, or exacerbation of symptoms in patients with pre-existing psychosis. Evaluate for bipolar disorder prior to stimulant use (5.4)
- *Suppression of Growth:* Monitor height and weight in pediatric patients during treatment (5.5)
- *Peripheral Vasculopathy, including Raynaud's phenomenon:* Stimulants are associated with peripheral vasculopathy, including Raynaud's phenomenon. Careful observation for digital changes is necessary during treatment with stimulants (5.6)
- *Serotonin Syndrome:* Increased risk when co-administered with serotonergic agents (e.g., SSRIs, SNRIs, triptans), but also during overdosage situations. If it occurs, discontinue lisdexamfetamine dimesylate capsule and initiate supportive treatment (4, 5.7, 10)

ADVERSE REACTIONS

Most common adverse reactions (incidence ≥5% and at a rate at least twice placebo) in pediatric patients ages 6 to 17 years, and/or adults with ADHD were anorexia, anxiety, decreased appetite, decreased weight, diarrhea, dizziness, dry mouth, irritability, insomnia, nausea, upper abdominal pain, and vomiting (6.1)

Most common adverse reactions (incidence ≥ 5% and at a rate at least twice placebo) in adults with BED were dry mouth, insomnia, decreased appetite, increased heart rate, constipation, feeling jittery, and anxiety (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Solco Healthcare US, LLC at 1-866-257-2597 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

DRUG INTERACTIONS

Acidifying and Alkalinizing Agents: Agents that alter urinary pH can alter blood levels of amphetamine. Acidifying agents decrease amphetamine blood levels, while alkalinizing agents increase amphetamine blood levels. Adjust lisdexamfetamine dimesylate capsules dosage accordingly (2.6, 7.1)

USE IN SPECIFIC POPULATIONS

- *Pregnancy:* May cause fetal harm (8.1)
- *Lactation:* Breastfeeding not recommended (8.2)

See 17 for PATIENT COUNSELING INFORMATION and Medication Guide.

Revised: 3/2023

FULL PRESCRIBING INFORMATION: CONTENTS*

WARNING: ABUSE AND DEPENDENCE
1 INDICATIONS AND USAGE

2 DOSAGE AND ADMINISTRATION
2.1 Pre-treatment Screening
2.2 General Instructions for Use
2.3 Dosage for Treatment of ADHD
2.4 Dosage for Treatment of Moderate to Severe BED in Adults
2.5 Dosage in Patients with Renal Impairment
2.6 Dosage Modifications due to Drug Interactions
3 DOSAGE FORMS AND STRENGTHS
4 CONTRAINDICATIONS
5 WARNINGS AND PRECAUTIONS
5.1 Potential for Abuse and Dependence
5.2 Serious Cardiovascular Reactions
5.3 Blood Pressure and Heart Rate Increases
5.4 Psychiatric Adverse Reactions
5.5 Suppression of Growth
5.6 Peripheral Vasculopathy, including Raynaud's Phenomenon
5.7 Serotonin Syndrome
6 ADVERSE REACTIONS
6.1 Clinical Trials Experience
6.2 Postmarketing Experience
7 DRUG INTERACTIONS
7.1 Drugs Having Clinically Important Interactions with Amphetamines
7.2 Drugs Having No Clinically Important Interactions with Lisdexamfetamine Dimesylate Capsules
8 USE IN SPECIFIC POPULATIONS
8.1 Pregnancy
8.2 Lactation
8.4 Pediatric Use
8.5 Geriatric Use
8.6 Renal Impairment
9 DRUG ABUSE AND DEPENDENCE
9.1 Controlled Substance
9.2 Abuse
9.3 Dependence
10 OVERDOSAGE
11 DESCRIPTION
12 CLINICAL PHARMACOLOGY
12.1 Mechanism of Action
12.2 Pharmacodynamics
12.3 Pharmacokinetics
13 NONCLINICAL TOXICOLOGY
13.1 Carcinogenesis, Mutagenesis, and Impairment of Fertility
13.2 Animal Toxicology and/or Pharmacology
14 CLINICAL STUDIES
14.1 Attention Deficit Hyperactivity Disorder (ADHD)
14.2 Binge Eating Disorder (BED)
16 HOW SUPPLIED/STORAGE AND HANDLING
16.1 How Supplied
16.2 Storage and Handling
17 PATIENT COUNSELING INFORMATION

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

FULL PRESCRIBING INFORMATION

WARNING: ABUSE AND DEPENDENCE

CNS stimulants, including lisdexamfetamine dimesylate, other amphetamine-containing products, and methylphenidate have a high potential for abuse and dependence. Assess the risk of abuse prior to prescribing and monitor for signs of abuse and dependence while on therapy *[see Warnings and Precautions (5.1), and Drug Abuse and Dependence (9.2, 9.3)].*

1 INDICATIONS AND USAGE

Lisdexamfetamine dimesylate capsules are indicated for the treatment of:

- Attention Deficit Hyperactivity Disorder (ADHD) in adults and pediatric patients 6 years and older *[see Clinical Studies (14.1)].*
- Moderate to severe binge eating disorder (BED) in adults *[see Clinical Studies (14.2)]*.

Limitations of Use:

- Pediatric patients with ADHD younger than 6 years of age experienced more long-term weight loss than patients 6 years and older *[see Use in Specific Populations (8.4)].*
- Lisdexamfetamine dimesylate capsules are not indicated or recommended for weight loss. Use of other sympathomimetic drugs for weight loss has been associated with serious cardiovascular adverse events. The safety and effectiveness of lisdexamfetamine dimesylate capsules for the treatment of obesity have not been established *[see Warnings and Precautions (5.2)].*

2 DOSAGE AND ADMINISTRATION

Click here to enter Dosage and Administration

2.1 Pre-treatment Screening

Prior to treating patients with CNS stimulants, including lisdexamfetamine dimesylate capsules, assess for the presence of cardiac disease (e.g., a careful history, family history of sudden death or ventricular arrhythmia, and physical exam) *[see Warnings and Precautions (5.2)]*.

To reduce the abuse of CNS stimulants including lisdexamfetamine dimesylate capsules, assess the risk of abuse, prior to prescribing. After prescribing, keep careful

prescription records, educate patients about abuse, monitor for signs of abuse and overdose, and re-evaluate the need for lisdexamfetamine dimesylate capsules use *[see Warnings and Precautions (5.1), Drug Abuse and Dependence (9)]*.

2.2 General Instructions for Use

Take lisdexamfetamine dimesylate capsules by mouth in the morning with or without food; avoid afternoon doses because of the potential for insomnia. Lisdexamfetamine dimesylate capsules may be administered in one of the following ways:

Information for lisdexamfetamine dimesylate capsules:

- Swallow lisdexamfetamine dimesylate capsules whole, or
- Open capsules, empty and mix the entire contents with yogurt, water, or orange juice. If the contents of the capsule include any compacted powder, a spoon may be used to break apart the powder. The contents should be mixed until completely dispersed. Consume the entire mixture **immediately**. It should not be stored. The active ingredient dissolves completely once dispersed; however, a film containing the inactive ingredients may remain in the glass or container once the mixture is consumed.

Lisdexamfetamine dimesylate capsules can be substituted with lisdexamfetamine dimesylate chewable tablets on a unit per unit/mg per mg basis (for example, 30 mg capsules for 30 mg chewable tablet) *[see Clinical Pharmacology (12.3)].*

Do not take anything less than one capsule per day. A single dose should not be divided.

2.3 Dosage for Treatment of ADHD

The recommended starting dosage in adults and pediatric patients 6 years and older is 30 mg once daily in the morning. Dosage may be adjusted in increments of 10 mg or 20 mg at approximately weekly intervals up to maximum recommended dosage of 70 mg once daily *[see Clinical Studies (14.1)]*.

2.4 Dosage for Treatment of Moderate to Severe BED in Adults

The recommended starting dosage in adults is 30 mg once daily to be titrated in increments of 20 mg at approximately weekly intervals to achieve the recommended target dose of 50 mg to 70 mg once daily. The maximum recommended dosage is 70 mg once daily *[see Clinical Studies (14.2)]*. Discontinue lisdexamfetamine dimesylate capsules if binge eating does not improve.

2.5 Dosage in Patients with Renal Impairment

In patients with severe renal impairment (GFR 15 to < 30 mL/min/1.73 m^2), the maximum dosage should not exceed 50 mg once daily. In patients with end stage renal disease (ESRD, GFR < 15 mL/min/1.73 m^2), the maximum recommended dosage is 30 mg once daily *[see Use in Specific Populations (8.6)]*.

2.6 Dosage Modifications due to Drug Interactions

Agents that alter urinary pH can impact urinary excretion and alter blood levels of amphetamine. Acidifying agents (e.g., ascorbic acid) decrease blood levels, while alkalinizing agents (e.g., sodium bicarbonate) increase blood levels. Adjust

lisdexamfetamine dimesylate capsules dosage accordingly *[see Drug Interactions (7.1)]*.

3 DOSAGE FORMS AND STRENGTHS

Lisdexamfetamine dimesylate capsules:

- Capsules 10 mg: SIZE “3” Capsule, opaque pink body/opaque pink cap (imprinted with S6 10)
- Capsules 20 mg: SIZE “3” Capsule, opaque ivory body/opaque ivory cap (imprinted with S6 20)
- Capsules 30 mg: SIZE “3” Capsule, opaque white body/opaque orange cap (imprinted with S6 30)
- Capsules 40 mg: SIZE “3” Capsule, opaque white body/opaque blue green cap (imprinted with S6 40)
- Capsules 50 mg: SIZE “3” Capsule, opaque white body/opaque blue cap (imprinted with S6 50)
- Capsules 60 mg: SIZE “3” Capsule, opaque aqua blue body/opaque aqua blue cap (imprinted with S6 60)
- Capsules 70 mg: SIZE “3” Capsule, opaque blue body/opaque orange cap (imprinted with S6 70)

4 CONTRAINDICATIONS

Lisdexamfetamine dimesylate capsules are contraindicated in patients with:

- Known hypersensitivity to amphetamine products or other ingredients of lisdexamfetamine dimesylate capsules. Anaphylactic reactions, Stevens-Johnson Syndrome, angioedema, and urticaria have been observed in postmarketing reports *[see Adverse Reactions (6.2)].*
- Patients taking monoamine oxidase inhibitors (MAOIs), or within 14 days of stopping MAOIs (including MAOIs such as linezolid or intravenous methylene blue), because of an increased risk of hypertensive crisis *[see Warnings and Precautions (5.7) and Drug Interactions (7.1)]*.

5 WARNINGS AND PRECAUTIONS

Click here to enter Warnings and Precautions

5.1 Potential for Abuse and Dependence

CNS stimulants, including lisdexamfetamine dimesylate, other amphetamine-containing products, and methylphenidate, have a high potential for abuse and dependence. Assess the risk of abuse prior to prescribing, and monitor for signs of abuse and dependence while on therapy *[see Drug Abuse and Dependence (9.2, 9.3)]*.

5.2 Serious Cardiovascular Reactions

Sudden death, stroke, and myocardial infarction have been reported in adults with CNS stimulant treatment at recommended doses. Sudden death has been reported in pediatric patients with structural cardiac abnormalities and other serious heart problems

taking CNS stimulants at recommended doses for ADHD. Avoid use in patients with known structural cardiac abnormalities, cardiomyopathy, serious heart arrhythmia, coronary artery disease, and other serious heart problems. Further evaluate patients who develop exertional chest pain, unexplained syncope, or arrhythmias during lisdexamfetamine dimesylate capsules treatment.

5.3 Blood Pressure and Heart Rate Increases

CNS stimulants cause an increase in blood pressure (mean increase about 2 to 4 mm Hg) and heart rate (mean increase about 3 to 6 bpm). Monitor all patients for potential tachycardia and hypertension.

5.4 Psychiatric Adverse Reactions

Exacerbation of Pre-existing Psychosis

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

Induction of a Manic Episode in Patients with Bipolar Disorder

CNS stimulants may induce a mixed/manic episode in patients with bipolar disorder. Prior to initiating treatment, screen patients for risk factors for developing a manic episode (e.g., comorbid or history of depressive symptoms or a family history of suicide, bipolar disorder, and depression).

New Psychotic or Manic Symptoms

CNS stimulants, at recommended doses, may cause psychotic or manic symptoms (e.g., hallucinations, delusional thinking, or mania) in patients without a prior history of psychotic illness or mania. If such symptoms occur, consider discontinuing lisdexamfetamine dimesylate capsules. In a pooled analysis of multiple short-term, placebo-controlled studies of CNS stimulants, psychotic or manic symptoms occurred in 0.1% of CNS stimulant-treated patients compared to 0% in placebo-treated patients.

5.5 Suppression of Growth

CNS stimulants have been associated with weight loss and slowing of growth rate in pediatric patients. Closely monitor growth (weight and height) in pediatric patients treated with CNS stimulants, including lisdexamfetamine dimesylate capsules. In a 4-week, placebo-controlled trial of lisdexamfetamine dimesylate capsules in pediatric patients ages 6 to 12 years old with ADHD, there was a dose-related decrease in weight in the lisdexamfetamine dimesylate capsules groups compared to weight gain in the placebo group. Additionally, in studies of another stimulant, there was slowing of the increase in height *[see Adverse Reactions (6.1)]*.

Patients who are not growing or gaining height or weight as expected may need to have their treatment interrupted. Lisdexamfetamine dimesylate capsules are not approved for use in pediatric patients below 6 years of age *[see Use in Specific Populations (8.4)].*

5.6 Peripheral Vasculopathy, including Raynaud’s Phenomenon

Stimulants, including lisdexamfetamine dimesylate capsules, are associated with peripheral vasculopathy, including Raynaud’s phenomenon. Signs and symptoms are usually intermittent and mild; however, very rare sequelae include digital ulceration

and/or soft tissue breakdown. Effects of peripheral vasculopathy, including Raynaud's phenomenon, were observed in post-marketing reports at different times and at therapeutic doses in all age groups throughout the course of treatment. Signs and symptoms generally improve after reduction in dose or discontinuation of drug. Careful observation for digital changes is necessary during treatment with stimulants. Further clinical evaluation (e.g., rheumatology referral) may be appropriate for certain patients.

5.7 Serotonin Syndrome

Serotonin syndrome, a potentially life-threatening reaction, may occur when amphetamines are used in combination with other drugs that affect the serotonergic neurotransmitter systems such as monoamine oxidase inhibitors (MAOIs), selective serotonin reuptake inhibitors (SSRIs), serotonin norepinephrine reuptake inhibitors (SNRIs), triptans, tricyclic antidepressants, fentanyl, lithium, tramadol, tryptophan, buspirone, and St. John's Wort *[see Drug Interactions (7.1)]*. The co-administration with cytochrome P450 2D6 (CYP2D6) inhibitors may also increase the risk with increased exposure to the active metabolite of lisdexamfetamine dimesylate capsules (dextroamphetamine). In these situations, consider an alternative non-serotonergic drug or an alternative drug that does not inhibit CYP2D6 *[see Drug Interactions (7.1)]*. Serotonin syndrome symptoms may include mental status changes (e.g., agitation, hallucinations, delirium, and coma), autonomic instability (e.g., tachycardia, labile blood pressure, dizziness, diaphoresis, flushing, hyperthermia), neuromuscular symptoms (e.g., tremor, rigidity, myoclonus, hyperreflexia, incoordination), seizures, and/or gastrointestinal symptoms (e.g., nausea, vomiting, diarrhea).

Concomitant use of lisdexamfetamine dimesylate capsules with MAOI drugs is contraindicated *[see Contraindications (4)]*.

Discontinue treatment with lisdexamfetamine dimesylate capsules and any concomitant serotonergic agents immediately if symptoms of serotonin syndrome occur, and initiate supportive symptomatic treatment. If concomitant use of lisdexamfetamine dimesylate capsules with other serotonergic drugs or CYP2D6 inhibitors is clinically warranted, initiate lisdexamfetamine dimesylate capsules with lower doses, monitor patients for the emergence of serotonin syndrome during drug initiation or titration, and inform patients of the increased risk for serotonin syndrome.

6 ADVERSE REACTIONS

The following adverse reactions are discussed in greater detail in other sections of the labeling:

- Known hypersensitivity to amphetamine products or other ingredients of lisdexamfetamine dimesylate capsules *[see Contraindications (4)]*
- Hypertensive Crisis When Used Concomitantly with Monoamine Oxidase Inhibitors *[see Contraindications (4) and Drug Interactions (7.1)]*
- Drug Dependence *[see Boxed Warning, Warnings and Precautions (5.1), and Drug Abuse and Dependence (9.2, 9.3)]*
- Serious Cardiovascular Reactions *[see Warnings and Precautions (5.2)]*
- Blood Pressure and Heart Rate Increases *[see Warnings and Precautions (5.3)]*
- Psychiatric Adverse Reactions *[see Warnings and Precautions (5.4)]*
- Suppression of Growth *[see Warnings and Precautions (5.5)]*

- Peripheral Vasculopathy, including Raynaud's phenomenon *[see Warnings and Precautions (5.6)]*
- Serotonin Syndrome *[see Warnings and Precautions (5.7)]*

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

Attention Deficit Hyperactivity Disorder

The safety data in this section is based on data from the 4-week controlled parallel-group clinical studies of lisdexamfetamine dimesylate capsules in pediatric and adult patients with ADHD *[see Clinical Studies (14.1)]*.

Adverse Reactions Associated with Discontinuation of Treatment in ADHD Clinical Trials

In the controlled trial in pediatric patients ages 6 to 12 years (Study 1), 8% (18/218) of lisdexamfetamine dimesylate capsules-treated patients discontinued due to adverse reactions compared to 0% (0/72) of placebo-treated patients. The most frequently reported adverse reactions (1% or more and twice rate of placebo) were ECG voltage criteria for ventricular hypertrophy, tic, vomiting, psychomotor hyperactivity, insomnia, decreased appetite and rash [2 instances for each adverse reaction, i.e., 2/218 (1%)]. Less frequently reported adverse reactions (less than 1% or less than twice rate of placebo) included abdominal pain upper, dry mouth, weight decreased, dizziness, somnolence, logorrhea, chest pain, anger and hypertension.

In the controlled trial in pediatric patients ages 13 to 17 years (Study 4), 3% (7/233) of lisdexamfetamine dimesylate capsules-treated patients discontinued due to adverse reactions compared to 1% (1/77) of placebo-treated patients. The most frequently reported adverse reactions (1% or more and twice rate of placebo) were decreased appetite (2/233; 1%) and insomnia (2/233; 1%). Less frequently reported adverse reactions (less than 1% or less than twice rate of placebo) included irritability, dermatillomania, mood swings, and dyspnea.

In the controlled adult trial (Study 7), 6% (21/358) of lisdexamfetamine dimesylate capsules-treated patients discontinued due to adverse reactions compared to 2% (1/62) of placebo-treated patients. The most frequently reported adverse reactions (1% or more and twice rate 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%). Less frequently reported adverse reactions (less than 1% or less than twice rate of placebo) included palpitations, diarrhea, nausea, decreased appetite, dizziness, agitation, depression, paranoia and restlessness.

Adverse Reactions Occurring at an Incidence of ≥5% or More Among Lisdexamfetamine Dimesylate Capsules Treated Patients with ADHD in Clinical Trials

The most common adverse reactions (incidence ≥5% and at a rate at least twice placebo) reported in pediatric patients ages 6 to 17 years, and/or adults were anorexia, anxiety, decreased appetite, decreased weight, diarrhea, dizziness, dry mouth, irritability, insomnia, nausea, upper abdominal pain, and vomiting.

Adverse Reactions Occurring at an Incidence of 2% or More Among Lisdexamfetamine Dimesylate Capsules Treated Patients with ADHD in Clinical Trials

Adverse reactions reported in the controlled trials in pediatric patients ages, 6 to 12 years (Study 1), pediatric patients ages 13 to 17 years (Study 4), and adult patients (Study 7) treated with lisdexamfetamine dimesylate capsules or placebo are presented in Tables 1, 2 and 3 below.

Table 1 Adverse Reactions Reported by 2% or More of Pediatric Patients Ages 6 to 12 Years with ADHD Taking Lisdexamfetamine Dimesylate Capsules and Greater than or Equal to Twice the Incidence in Patients Taking Placebo in a 4-Week Clinical Trial (Study 1)

	Lisdexamfetamine dimesylate capsules (n=218)	Placebo (n=72)
Decreased Appetite	39%	4%
Insomnia	22%	3%
Abdominal Pain Upper	12%	6%
Irritability	10%	0%
Vomiting	9%	4%
Weight Decreased	9%	1%
Nausea	6%	3%
Dry Mouth	5%	0%
Dizziness	5%	0%
Affect lability	3%	0%
Rash	3%	0%
Pyrexia	2%	1%
Somnolence	2%	1%
Tic	2%	0%
Anorexia	2%	0%

Table 2 Adverse Reactions Reported by 2% or More of Pediatric Patients Ages 13 to 17 Years with ADHD Taking Lisdexamfetamine Dimesylate Capsules and Greater than or Equal to Twice the Incidence in Patients Taking Placebo in a 4-Week Clinical Trial (Study 4)

	Lisdexamfetamine dimesylate capsules (n=233)	Placebo (n=77)
Decreased Appetite	34%	3%
Insomnia	13%	4%
Weight Decreased	9%	0%
Dry Mouth	4%	1%
Palpitations	2%	1%
Anorexia	2%	0%
Tremor	2%	0%

Table 3 Adverse Reactions Reported by 2% or More of Adult Patients with ADHD Taking Lisdexamfetamine Dimesylate Capsules and Greater than or Equal to Twice the Incidence in Patients Taking Placebo in a 4-Week Clinical

Trial (Study 7)

	Lisdexamfetamine dimesylate capsules (n=358)	Placebo (n=62)
Decreased Appetite	27%	2%
Insomnia	27%	8%
Dry Mouth	26%	3%
Diarrhea	7%	0%
Nausea	7%	0%
Anxiety	6%	0%
Anorexia	5%	0%
Feeling Jittery	4%	0%
Agitation	3%	0%
Increased Blood Pressure	3%	0%
Hyperhidrosis	3%	0%
Restlessness	3%	0%
Decreased Weight	3%	0%
Dyspnea	2%	0%
Increased Heart Rate	2%	0%
Tremor	2%	0%
Palpitations	2%	0%

In addition, in the adult population erectile dysfunction was observed in 2.6% of males on lisdexamfetamine dimesylate capsules and 0% on placebo; decreased libido was observed in 1.4% of subjects on lisdexamfetamine dimesylate capsules and 0% on placebo.

Weight Loss and Slowing Growth Rate in Pediatric Patients with ADHD

In a controlled trial of lisdexamfetamine dimesylate capsules in pediatric patients ages 6 to 12 years (Study 1), mean weight loss from baseline after 4 weeks of therapy was -0.9, -1.9, and -2.5 pounds, respectively, for patients receiving 30 mg, 50 mg, and 70 mg of lisdexamfetamine dimesylate capsules, compared to a 1 pound 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 pediatric patients ages 6 to 12 years who received lisdexamfetamine dimesylate capsules over 12 months suggests that consistently medicated pediatric patients (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 60.9 and 47.2, respectively). In a 4-week controlled trial of lisdexamfetamine dimesylate capsules in pediatric patients 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 lisdexamfetamine dimesylate capsules, compared to a 2.0 pound weight gain for patients receiving placebo.

Careful follow-up of weight and height in pediatric patients 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 pediatric patients over 36 months (to the ages of 10 to 13 years), suggests that consistently medicated pediatric patients ages 7 to 13 years (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 pediatric patients ages 13 to 17 years, mean weight change from baseline within the initial 4 weeks of therapy was -1.1 pounds and -2.8 pounds, 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 *[see Warnings and Precautions (5.5)]*.

Weight Loss in Adults with ADHD

In the controlled adult trial (Study 7), mean weight loss after 4 weeks of therapy was 2.8 pounds, 3.1 pounds, and 4.3 pounds, for patients receiving final doses of 30 mg, 50 mg, and 70 mg of lisdexamfetamine dimesylate capsules, respectively, compared to a mean weight gain of 0.5 pounds for patients receiving placebo.

Binge Eating Disorder

The safety data in this section is based on data from two 12-week parallel group, flexible-dose, placebo-controlled studies in adults with BED *[see Clinical Studies 14.2]*. Patients with cardiovascular risk factors other than obesity and smoking were excluded.

Adverse Reactions Associated with Discontinuation of Treatment in BED Clinical Trials

In controlled trials of patients ages 18 to 55 years, 5.1% (19/373) of lisdexamfetamine dimesylate capsules-treated patients discontinued due to adverse reactions compared to 2.4% (9/372) of placebo-treated patients. No single adverse reaction led to discontinuation in 1% or more of lisdexamfetamine dimesylate capsules-treated patients. Less commonly reported adverse reactions (less than 1% or less than twice rate of placebo) included increased heart rate, headache, abdominal pain upper, dyspnea, rash, insomnia, irritability, feeling jittery and anxiety.

Adverse Reactions Occurring at an Incidence of 5% or More and At Least Twice Placebo Among Lisdexamfetamine Dimesylate Capsules Treated Patients with BED in Clinical Trials

The most common adverse reactions (incidence ≥5% and at a rate at least twice placebo) reported in adults were dry mouth, insomnia, decreased appetite, increased heart rate, constipation, feeling jittery, and anxiety.

Adverse Reactions Occurring at an Incidence of 2% or More and At Least Twice Placebo Among Lisdexamfetamine Dimesylate Capsules Treated Patients with BED in Clinical Trials

Adverse reactions reported in the pooled controlled trials in adult patients (Study 11 and 12) treated with lisdexamfetamine dimesylate capsules or placebo are presented in Table 4 below.

Table 4 Adverse Reactions Reported by 2% or More of Adult Patients with BED Taking Lisdexamfetamine Dimesylate Capsules and Greater than or Equal to Twice the Incidence in Patients Taking Placebo in 12-Week Clinical Trials (Study 11 and 12)

	Lisdexamfetamine dimesylate capsules	Placebo (N=372)

	(N=373)	
Dry Mouth	36%	7%
Insomnia[1]	20%	8%
Decreased Appetite	8%	2%
Increased Heart Rate[2]	7%	1%
Feeling Jittery	6%	1%
Constipation	6%	1%
Anxiety	5%	1%
Diarrhea	4%	2%
Decreased Weight	4%	0%
Hyperhidrosis	4%	0%
Vomiting	2%	1%
Gastroenteritis	2%	1%
Paresthesia	2%	1%
Pruritus	2%	1%
Upper Abdominal Pain	2%	0%
Energy Increased	2%	0%
Urinary Tract Infection	2%	0%
Nightmare	2%	0%
Restlessness	2%	0%
Oropharyngeal Pain	2%	0%

[1] Includes all preferred terms containing the word “insomnia.”
[2] Includes the preferred terms “heart rate increased” and “tachycardia.”

6.2 Postmarketing Experience

The following adverse reactions have been identified during postapproval use of lisdexamfetamine dimesylate capsules. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure. These events are as follows: cardiomyopathy, mydriasis, diplopia, difficulties with visual accommodation, blurred vision, eosinophilic hepatitis, anaphylactic reaction, hypersensitivity, dyskinesia, dysgeusia, tics, bruxism, depression, dermatillomania, alopecia, aggression, Stevens-Johnson Syndrome, chest pain, angioedema, urticaria, seizures, libido changes, frequent or prolonged erections, constipation, rhabdomyolysis, and intestinal ischemia.

7 DRUG INTERACTIONS

Click here to enter Drug Interactions

7.1 Drugs Having Clinically Important Interactions with Amphetamines

Table 5 Drugs having clinically important interactions with amphetamines.

MAO Inhibitors (MAOI)	
Clinical Impact	MAOI antidepressants slow amphetamine metabolism, increasing amphetamines effect on the release of norepinephrine and other monoamines from adrenergic nerve endings causing headaches and other signs of hypertensive crisis. Toxic neurological effects and malignant hyperpyrexia

	can occur, sometimes with fatal results.
Intervention	Do not administer lisdexamfetamine dimesylate capsules during or within 14 days following the administration of MAOI [see *Contraindications (4)*].
Serotonergic Drugs	
Clinical Impact	The concomitant use of lisdexamfetamine dimesylate capsules and serotonergic drugs increases the risk of serotonin syndrome.
Intervention	Initiate with lower doses and monitor patients for signs and symptoms of serotonin syndrome, particularly during lisdexamfetamine dimesylate capsules initiation or dosage increase. If serotonin syndrome occurs, discontinue lisdexamfetamine dimesylate capsules and the concomitant serotonergic drug(s) *[see Warnings and Precautions (5.7)]*.
CYP2D6 Inhibitors	
Clinical Impact	The concomitant use of lisdexamfetamine dimesylate capsules and CYP2D6 inhibitors may increase the exposure of dextroamphetamine, the active metabolite of lisdexamfetamine dimesylate capsules compared to the use of the drug alone and increase the risk of serotonin syndrome.
Intervention	Initiate with lower doses and monitor patients for signs and symptoms of serotonin syndrome particularly during lisdexamfetamine dimesylate capsules initiation and after a dosage increase. If serotonin syndrome occurs, discontinue lisdexamfetamine dimesylate capsules and the CYP2D6 inhibitor *[see Warnings and Precautions (5.7) and Overdosage (10)]*.
Alkalinizing Agents	
Clinical Impact	Urinary alkalinizing agents can increase blood levels and potentiate the action of amphetamine.
Intervention	Co-administration of lisdexamfetamine dimesylate capsules and urinary alkalinizing agents should be avoided.
Acidifying Agents	
Clinical Impact	Urinary acidifying agents can lower blood levels and efficacy of amphetamines.
Intervention	Increase dose based on clinical response.
Tricyclic Antidepressants	
Clinical Impact	May enhance the activity of tricyclic or sympathomimetic agents causing striking and sustained increases in the concentration of d-amphetamine in the brain; cardiovascular effects can be potentiated.
Intervention	Monitor frequently and adjust or use alternative therapy based on clinical response.

7.2 Drugs Having No Clinically Important Interactions with Lisdexamfetamine Dimesylate Capsules

From a pharmacokinetic perspective, no dose adjustment of lisdexamfetamine dimesylate capsules is necessary when lisdexamfetamine dimesylate capsules are co-administered with guanfacine, venlafaxine, or omeprazole. In addition, no dose

adjustment of guanfacine or venlafaxine is needed when lisdexamfetamine dimesylate capsules are co-administered *[see Clinical Pharmacology (12.3)]*.

From a pharmacokinetic perspective, no dose adjustment for drugs that are substrates of CYP1A2 (e.g., theophylline, duloxetine, melatonin), CYP2D6 (e.g., atomoxetine, desipramine, venlafaxine), CYP2C19 (e.g., omeprazole, lansoprazole, clobazam), and CYP3A4 (e.g., midazolam, pimozide, simvastatin) is necessary when lisdexamfetamine dimesylate capsules are co-administered *[see Clinical Pharmacology (12.3)]*.

8 USE IN SPECIFIC POPULATIONS

Click here to enter Use in Specific Populations

8.1 Pregnancy

Pregnancy Exposure Registry

There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to ADHD medications during pregnancy. Healthcare providers are encouraged to register patients by calling the National Pregnancy Registry for Psychostimulants at 1-866-961-2388 or visiting online at https://womensmentalhealth.org/research/pregnancyregistry/adhd-medications/

Risk Summary

The limited available data from published literature and postmarketing reports on use of lisdexamfetamine dimesylate capsules in pregnant women are not sufficient to inform a drug-associated risk for major birth defects and miscarriage. Adverse pregnancy outcomes, including premature delivery and low birth weight, have been seen in infants born to mothers dependent on amphetamines *[see Clinical Considerations]*. In animal reproduction studies, lisdexamfetamine dimesylate (a prodrug of d-amphetamine) had no effects on embryo-fetal morphological development or survival when administered orally to pregnant rats and rabbits throughout the period of organogenesis. Pre- and postnatal studies were not conducted with lisdexamfetamine dimesylate. However, amphetamine (d- to l- ratio of 3:1) administration to pregnant rats during gestation and lactation caused a decrease in pup survival and a decrease in pup body weight that correlated with a delay in developmental landmarks at clinically relevant doses of amphetamine. In addition, adverse effects on reproductive performance were observed in pups whose mothers were treated with amphetamine. Long-term neurochemical and behavioral effects have also been reported in animal developmental studies using clinically relevant doses of amphetamine *[see Data]*.

The estimated background risk of major birth defects and miscarriage for the indicated population is unknown. All pregnancies have a background risk of birth defect, loss or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2-4% and 15-20%, respectively.

Clinical Considerations

Fetal/Neonatal Adverse Reactions

Amphetamines, such as lisdexamfetamine dimesylate capsules, cause vasoconstriction and thereby may decrease placental perfusion. In addition, amphetamines can stimulate

uterine contractions increasing the risk of premature delivery. Infants born to amphetamine-dependent mothers have an increased risk of premature delivery and low birth weight.

Monitor infants born to mothers taking amphetamines for symptoms of withdrawal such as feeding difficulties, irritability, agitation, and excessive drowsiness.

Data

Animal Data

Lisdexamfetamine dimesylate had no apparent effects on embryo-fetal morphological development or survival when administered orally to pregnant rats and rabbits throughout the period of organogenesis at doses of up to 40 and 120 mg/kg/day, respectively. These doses are approximately 5.5 and 33 times, respectively, the maximum recommended human dose (MRHD) of 70 mg/day given to adults, on a mg/m^2 body surface area basis.

A study was conducted with amphetamine (d- to l- enantiomer ratio of 3:1) in which pregnant rats received daily oral doses of 2, 6, and 10 mg/kg from gestation day 6 to lactation day 20. All doses caused hyperactivity and decreased weight gain in the dams. A decrease in pup survival was seen at all doses. A decrease in pup body weight was seen at 6 and 10 mg/kg which correlated with delays in developmental landmarks, such as preputial separation and vaginal opening. Increased pup locomotor activity was seen at 10 mg/kg on day 22 postpartum but not at 5 weeks postweaning. When pups were tested for reproductive performance at maturation, gestational weight gain, number of implantations, and number of delivered pups were decreased in the group whose mothers had been given 10 mg/kg.

A number of studies from the literature 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.

8.2 Lactation

Risk Summary

Lisdexamfetamine is a pro-drug of dextroamphetamine. Based on limited case reports in published literature, amphetamine (d-or d, l-) is present in human milk, at relative infant doses of 2% to 13.8% of the maternal weight-adjusted dosage and a milk/plasma ratio ranging between 1.9 and 7.5. There are no reports of adverse effects on the breastfed infant. Long-term neurodevelopmental effects on infants from amphetamine exposure are unknown. It is possible that large dosages of dextroamphetamine might interfere with milk production, especially in women whose lactation is not well established. Because of the potential for serious adverse reactions in nursing infants, including serious cardiovascular reactions, blood pressure and heart rate increase, suppression of growth, and peripheral vasculopathy, advise patients that breastfeeding is not recommended during treatment with lisdexamfetamine dimesylate capsules.

8.4 Pediatric Use

ADHD

Safety and effectiveness of lisdexamfetamine dimesylate capsules have been established in pediatric patients with ADHD ages 6 to 17 years *[see Dosage and Administration (2.3), Adverse Reactions (6.1), Clinical Pharmacology (12.3), and Clinical Studies (14.1)]*.

Safety and effectiveness of lisdexamfetamine dimesylate capsules have not been established in pediatric patients below the age of 6 years.

Safety and efficacy of lisdexamfetamine dimesylate capsules were evaluated in a double-blind, randomized, parallel-group, placebo-controlled, fixed-dose study in pediatric patients ages 4 to 5 years with ADHD, followed by a 1-year open-label extension study. In these studies, patients experienced elevated rates of adverse reactions, including weight loss, decreased BMI, decreased appetite, insomnia, infections (upper respiratory and nasopharyngitis), irritability, and affect lability.

With the same lisdexamfetamine dimesylate capsules dose, mean steady state exposure of dextroamphetamine was approximately 44% higher in pediatric patients ages 4 to 5 years compared to the pediatric patients ages 6 to 11 years.

BED

Safety and effectiveness of lisdexamfetamine dimesylate capsules have not been established in patients less than 18 years of age.

Growth Suppression

Growth should be monitored during treatment with stimulants, including lisdexamfetamine dimesylate capsules, and pediatric patients who are not growing or gaining weight as expected may need to have their treatment interrupted *[see Warnings and Precautions (5.5)and Adverse Reactions (6.1)]*.

Juvenile Animal Data

Studies conducted in juvenile rats and dogs at clinically relevant doses showed growth suppression that partially or fully reversed in dogs and female rats but not in male rats after a four-week drug-free recovery period.

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 for a child. 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 for a child). This effect partially or fully reversed during a four- week drug-free recovery period.

8.5 Geriatric Use

Clinical studies of lisdexamfetamine dimesylate capsules did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently

from younger subjects. Other reported clinical experience and pharmacokinetic data *[see Clinical Pharmacology (12.3)]* have not identified differences in responses between the elderly and younger patients. In general, dose selection for an elderly patient should start at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy.

8.6 Renal Impairment

Due to reduced clearance in patients with severe renal impairment (GFR 15 to < 30 mL/min/1.73 m^2), the maximum dose should not exceed 50 mg/day. The maximum recommended dose in ESRD (GFR < 15 mL/min/1.73 m^2) patients is 30 mg/day *[see Clinical Pharmacology (12.3)]*.

Lisdexamfetamine and d-amphetamine are not dialyzable.

9 DRUG ABUSE AND DEPENDENCE

Click here to enter Drug Abuse and Dependence

9.1 Controlled Substance

Lisdexamfetamine dimesylate capsules contain lisdexamfetamine, a prodrug of amphetamine, a Schedule II controlled substance.

9.2 Abuse

CNS stimulants, including lisdexamfetamine dimesylate, other amphetamines-containing products, and methylphenidate have a high potential for abuse. Abuse is the intentional non-therapeutic use of a drug, even once, to achieve a desired psychological or physiological effect. Abuse is characterized by impaired control over drug use, compulsive use, continued use despite harm, and craving. Drug addiction is a cluster of behavioral, cognitive, and physiological phenomena that may include a strong desire to take the drug, difficulties in controlling drug use (e.g., continuing drug use despite harmful consequences, giving higher priority to drug use than other activities and obligations), and possible tolerance or physical dependence. Both abuse and misuse may lead to addiction, and some individuals may develop addiction even when taking lisdexamfetamine dimesylate capsules as prescribed.

Signs and symptoms of amphetamine abuse may include increased heart rate, respiratory rate, blood pressure, and/or sweating, dilated pupils, hyperactivity, restlessness, insomnia, decreased appetite, loss of coordination, tremors, flushed skin, vomiting, and/or abdominal pain. Anxiety, psychosis, hostility, aggression, suicidal or homicidal ideation have also been seen. Abusers of CNS stimulants may chew, snort, inject, or use other unapproved routes of administration which can result in overdose and death *[see Overdosage (10)]*.

To reduce the abuse of CNS stimulants, including lisdexamfetamine dimesylate capsules, assess the risk of abuse prior to prescribing. After prescribing, keep careful prescription records, educate patients and their families about abuse and on proper storage and disposal of CNS stimulants. Monitor for signs of abuse while on therapy, and re-evaluate the need for lisdexamfetamine dimesylate capsules use.

<u>Studies of Lisdexamfetamine Dimesylate Capsules in Drug Abusers</u>

A randomized, double-blind, placebo-control, cross-over, abuse liability study in 38 patients with a history of drug abuse was conducted with single-doses of 50, 100, or 150 mg of lisdexamfetamine dimesylate capsules, 40 mg of immediate-release d-amphetamine sulphate (a controlled II substance), and 200 mg of diethylpropion hydrochloride (a controlled IV substance). Lisdexamfetamine dimesylate capsules 100 mg produced significantly less “Drug Liking Effects” as measured by the Drug Rating Questionnaire-Subject score, compared to d-amphetamine 40 mg; and 150 mg of lisdexamfetamine dimesylate capsules demonstrated similar “Drug-Liking Effects” compared to 40 mg of d-amphetamine and 200 mg of diethylpropion.

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.

9.3 Dependence

Physical Dependence

Lisdexamfetamine dimesylate capsules may produce physical dependence from continued therapy. Physical dependence is a state of adaptation manifested by a withdrawal syndrome produced by abrupt cessation, rapid dose reduction, or administration of an antagonist. Withdrawal symptoms after abrupt cessation following prolonged high-dosage administration of CNS stimulants include extreme fatigue and depression.

Tolerance

Lisdexamfetamine dimesylate capsules may produce tolerance from continued therapy. Tolerance is a state of adaptation in which exposure to a specific dose of a drug results in a reduction of the drug’s desired and/or undesired effects over time.

10 OVERDOSAGE

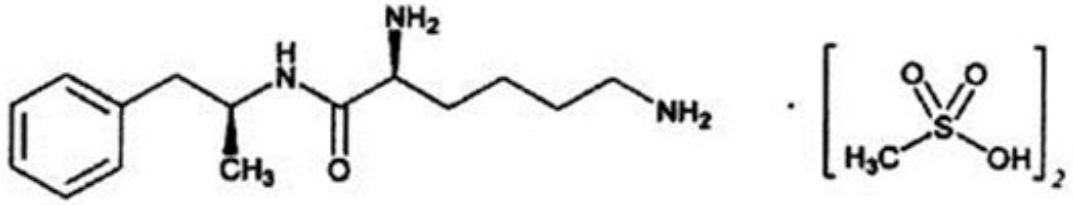
Consult with a Certified Poison Control Center (1-800-222-1222) for up-to-date guidance and advice for treatment of overdosage. Individual patient response to amphetamines varies widely. Toxic symptoms may occur idiosyncratically at low doses.

Manifestations of amphetamine overdose include restlessness, tremor, hyperreflexia, rapid respiration, confusion, assaultiveness, hallucinations, panic states, hyperpyrexia and rhabdomyolysis. Fatigue and depression usually follow the central nervous system stimulation. Serotonin syndrome has been reported with amphetamine use, including lisdexamfetamine dimesylate capsules. 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.

Lisdexamfetamine and d-amphetamine are not dialyzable.

11 DESCRIPTION

Lisdexamfetamine dimesylate capsules (lisdexamfetamine dimesylate), a CNS stimulant, are for once-a-day oral administration. The chemical designation for lisdexamfetamine dimesylate is (2S)-2,6-diamino-*N*-[(1*S*)-1-methyl-2-phenylethyl] hexanamide dimethanesulfonate. The molecular formula is $C_{15}H_{25}N_3O \bullet (CH_4O_3S)_2$, 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).

Information for lisdexamfetamine dimesylate capsules:

Lisdexamfetamine dimesylate capsules contain 10 mg, 20 mg, 30 mg, 40 mg, 50 mg, 60 mg, and 70 mg of lisdexamfetamine dimesylate (equivalent to 5.8 mg, 11.6 mg, 17.3 mg, 23.1 mg, 28.9 mg, 34.7 mg, and 40.5 mg of lisdexamfetamine).

Inactive ingredients: croscarmellose sodium, microcrystalline cellulose, and magnesium stearate.

The imprinting ink for all strengths contain D&C yellow #10 Aluminum Lake, FD&C Blue #1 Aluminum Lake, FD&C Blue #2 Aluminum Lake, FD&C Red #40 Aluminum Lake, iron oxide black, potassium hydroxide, propylene glycol and shellac glaze.

The capsule shells of each strength contain ingredients as below:

Strength	**Ingredients**
10 mg	FD&C Blue 1, FD&C Red 3, gelatin, titanium dioxide and sodium lauryl sulfate
20 mg	Iron Oxide Yellow, gelatin, titanium dioxide and sodium lauryl sulfate
30 mg	FD&C Red 3, FD&C Yellow 6, gelatin, titanium dioxide and sodium lauryl sulfate
40 mg	FD&C Blue 1, Iron Oxide Black, Iron Oxide Yellow, gelatin, titanium dioxide and sodium lauryl sulfate
50 mg	FD&C Blue 1, gelatin, titanium dioxide and sodium lauryl sulfate
60 mg	FD&C Blue 1, gelatin, titanium dioxide and sodium lauryl sulfate
70 mg	FD&C Blue 1, FD&C Red 3, FD&C Yellow 6, gelatin, titanium dioxide and sodium lauryl sulfate

12 CLINICAL PHARMACOLOGY

Click here to enter Clinical Pharmacology

12.1 Mechanism of Action

Lisdexamfetamine is a prodrug of dextroamphetamine. Amphetamines are non-catecholamine sympathomimetic amines with CNS stimulant activity. The exact mode of therapeutic action in ADHD and BED is not known.

12.2 Pharmacodynamics

Amphetamines 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 after oral administration of lisdexamfetamine dimesylate have been conducted in healthy adult (capsule formulation) and pediatric (6 to 12 years) patients with ADHD (capsule formulation). After single dose administration of lisdexamfetamine dimesylate, pharmacokinetics of dextroamphetamine was found to be linear between 30 mg and 70 mg in a pediatric study (6 to 12 years), and between 50 mg and 250 mg in an adult study. Dextroamphetamine pharmacokinetic parameters following administration of lisdexamfetamine dimesylate in adults exhibited low inter-subject (<25%) and intra-subject (<8%) variability. There is no accumulation of lisdexamfetamine and dextroamphetamine at steady state in healthy adults.

Absorption

Capsule formulation

Following single-dose oral administration of lisdexamfetamine dimesylate capsule (30 mg, 50 mg, or 70 mg) in patients ages 6 to 12 years with ADHD under fasted conditions, T_{max} of lisdexamfetamine and dextroamphetamine was reached at approximately 1 hour and 3.5 hours post dose, respectively. Weight/Dose normalized AUC and C_{max} values were the same in pediatric patients ages 6 to 12 years as the adults following single doses of 30 mg to 70 mg lisdexamfetamine dimesylate capsule.

Effect of food on capsule formulation

Neither food (a high fat meal or yogurt) nor orange juice affects the observed AUC and C_{max} of dextroamphetamine in healthy adults after single-dose oral administration of 70 mg of lisdexamfetamine dimesylate capsules. Food prolongs T_{max} by approximately 1 hour (from 3.8 hours at fasted state to 4.7 hours after a high fat meal or to 4.2 hours with yogurt). After an 8-hour fast, the AUC for dextroamphetamine following oral administration of lisdexamfetamine dimesylate in solution and as intact capsules were equivalent.

Elimination

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 volunteers ages 6 years and older. The plasma elimination half-life of dextroamphetamine was approximately 8.6 to 9.5 hours in pediatric patients 6 to 12 years and 10 to 11.3 hours in healthy adults.

Metabolism

Lisdexamfetamine is converted to dextroamphetamine and l-lysine primarily in blood due

to the hydrolytic activity of red blood cells after oral administration of lisdexamfetamine dimesylate. *In vitro* data demonstrated that red blood cells have a high capacity for metabolism of lisdexamfetamine; substantial hydrolysis occurred even at low hematocrit levels (33% of normal). Lisdexamfetamine is not metabolized by cytochrome P450 enzymes.

Excretion

Following 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.

Specific Populations

Exposures of dextroamphetamine in specific populations are summarized in Figure 1.

Figure 1: Specific Populations*:

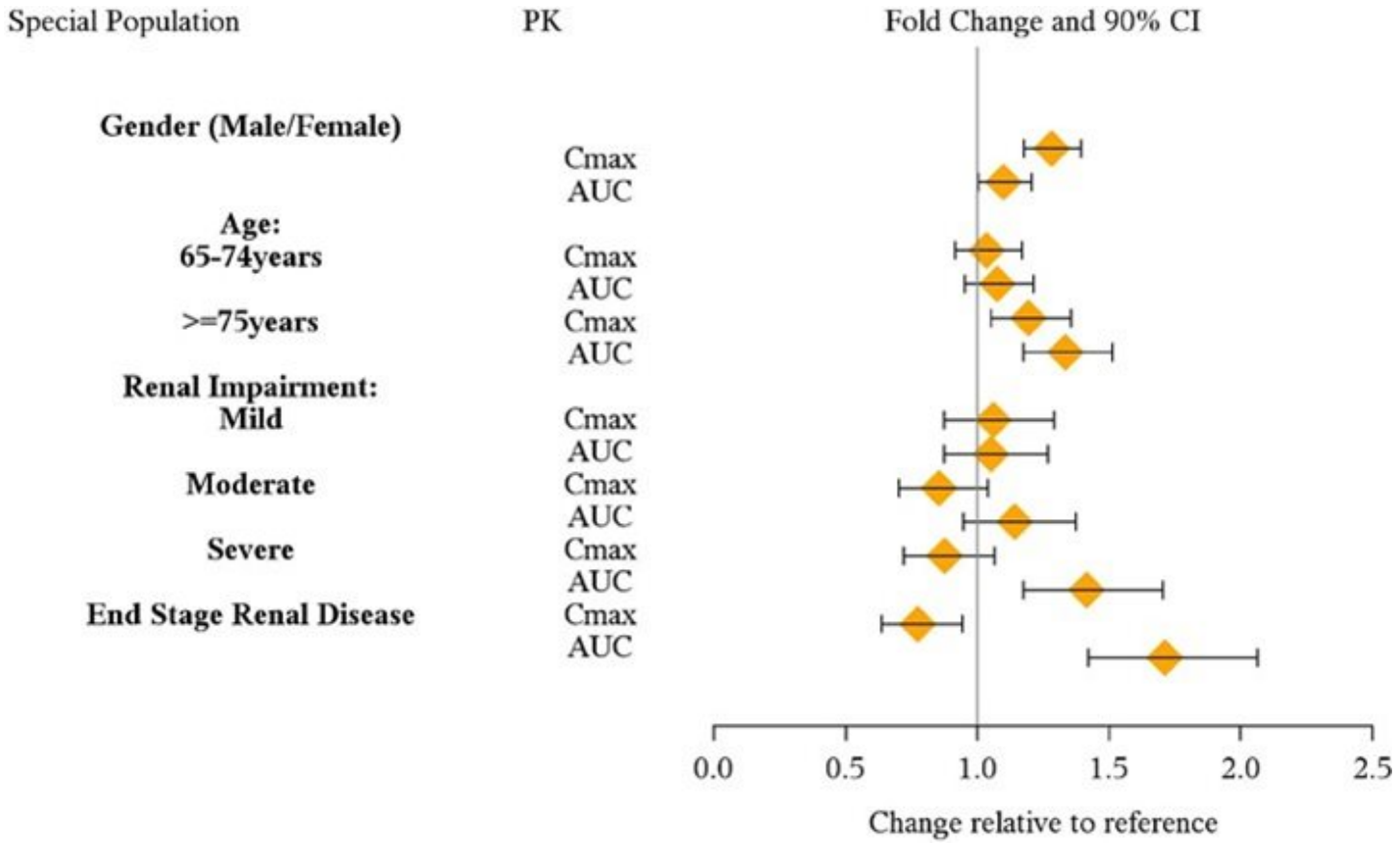
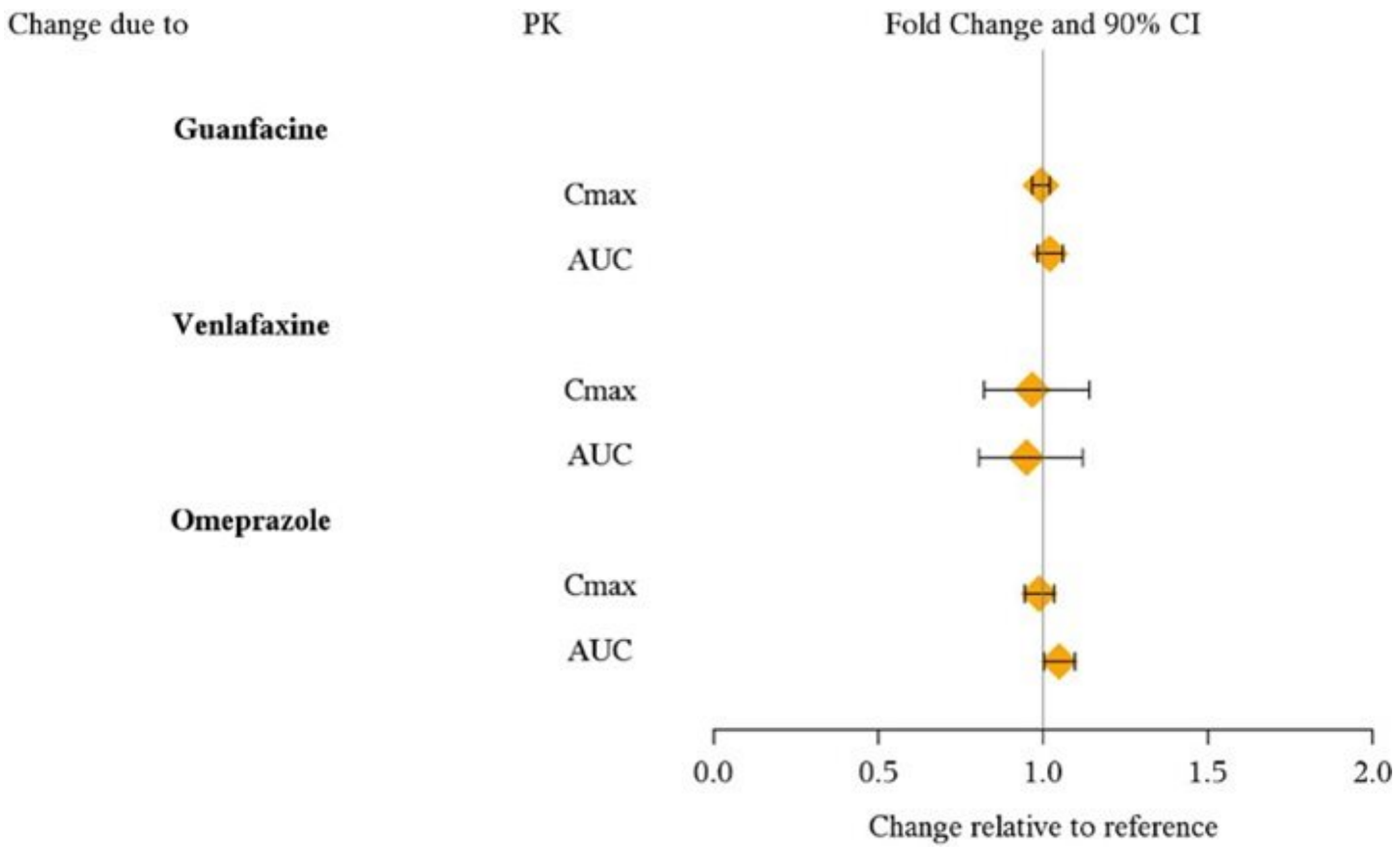


*Figure 1 shows the geometric mean ratios and the 90% confidence limits for C_{max} and AUC of d-amphetamine. Comparison for gender uses males as the reference. Comparison for age uses 55-64 years as the reference.

Drug Interaction Studies

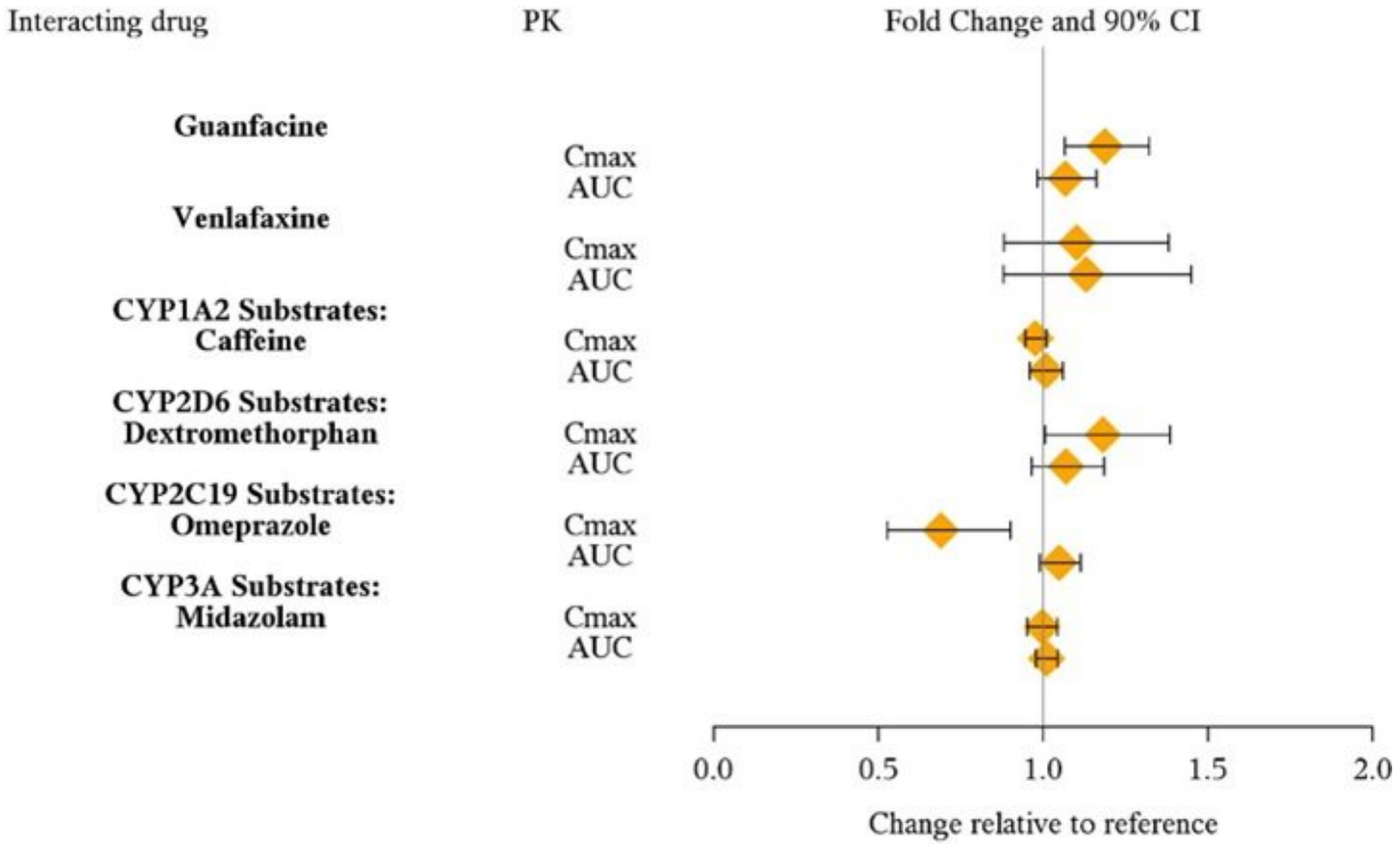
Effects of other drugs on the exposures of dextroamphetamine are summarized in Figure 2.

Figure 2: Effect of Other Drugs on Lisdexamfetamine Dimesylate Capsules:



The effects of lisdexamfetamine dimesylate capsules on the exposures of other drugs are summarized in Figure 3.

Figure 3: Effect of Lisdexamfetamine Dimesylate Capsules on Other Drugs:



13 NONCLINICAL TOXICOLOGY

Click here to enter Nonclinical Toxicology

13.1 Carcinogenesis, Mutagenesis, and Impairment of Fertility

Carcinogenesis

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.

Mutagenesis

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*.

Impairment of Fertility

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 and/or Pharmacology

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

Click here to enter Clinical Studies

14.1 Attention Deficit Hyperactivity Disorder (ADHD)

Pediatric Patients Ages 6 to 12 Years with ADHD

A double-blind, randomized, placebo-controlled, parallel-group study (Study 1) was conducted in pediatric patients ages 6 to 12 years (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 lisdexamfetamine dimesylate capsules or placebo once daily in the morning for a total of four weeks of treatment. All patients receiving lisdexamfetamine dimesylate capsules were initiated on 30 mg for the first week of treatment. Patients 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), an 18-item questionnaire with a score range of 0-54 points that measures the core symptoms of ADHD which includes both hyperactive/impulsive and inattentive subscales. Endpoint was defined as the last post-randomization treatment week (i.e., Weeks 1 through 4) for which a valid score was obtained. All lisdexamfetamine dimesylate capsules dose groups were superior to placebo in the primary efficacy outcome. Mean effects at all doses were similar; however, the highest dose (70 mg/day) was numerically superior to both lower doses (Study 1 in Table 6). 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 (Study 2) was conducted in pediatric patients ages 6 to 12 years (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 optimization with Adderall XR®, patients were randomly assigned to continue their optimized dose of Adderall XR (10 mg, 20 mg, or 30 mg), lisdexamfetamine dimesylate capsules (30 mg, 50 mg, or 70 mg), or placebo once daily in the morning for 1 week each treatment. Efficacy assessments were conducted at 1, 2, 3, 4.5, 6, 8, 10, and 12 hours post-dose using the Swanson, Kotkin, Agler, M.Flynn, and Pelham Deportment scores (SKAMP-DS), a 4-item subscale of the SKAMP with scores ranging from 0 to 24 points that measures deportment problems leading to classroom disruptions. A significant difference in patient behavior, based upon the average of investigator ratings on the SKAMP-DS across the 8 assessments were observed between patients when they received lisdexamfetamine dimesylate capsules compared to patients when they received placebo (Study 2 in Table 6). The drug effect reached statistical significance from hours 2 to 12 post-dose, but was not significant at 1 hour.

A second double-blind, placebo-controlled, randomized, crossover design, analog classroom study (Study 3) was conducted in pediatric patients ages 6 to 12 years (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 optimization with lisdexamfetamine dimesylate capsules (30 mg, 50 mg, 70 mg), patients were randomly assigned to continue their optimized dose of lisdexamfetamine dimesylate capsules 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 when they received lisdexamfetamine dimesylate capsules compared to patients when they received placebo (Study 3 in Table 6, Figure 4).

Pediatric Patients Ages 13 to 17 Years with ADHD

A double-blind, randomized, placebo-controlled, parallel-group study (Study 4) was conducted in pediatric patients ages 13 to 17 years (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 lisdexamfetamine dimesylate capsules (30 mg/day, 50 mg/day or 70 mg/day) or placebo for a total of four weeks of treatment. All patients receiving lisdexamfetamine dimesylate capsules were initiated on 30 mg for the first week of treatment. Patients 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). Endpoint was defined as the last post-randomization treatment week (i.e., Weeks 1 through 4) for which a valid score was obtained. All lisdexamfetamine dimesylate capsules dose groups were superior to placebo in the primary efficacy outcome (Study 4 in Table 6).

Pediatric Patients Ages 6 to 17 Years: Short-Term Treatment in ADHD

A double-blind, randomized, placebo- and active-controlled parallel-group, dose-optimization study (Study 5) was conducted in pediatric patients ages 6 to 17 years (n=336) who met DSM-IV criteria for ADHD. In this eight-week study, patients were randomized to a daily morning dose of lisdexamfetamine dimesylate capsules (30, 50 or 70 mg/day), an active control, or placebo (1:1:1). The study consisted of a Screening and Washout Period (up to 42 days), a 7-week Double-blind Evaluation Period (consisting of a 4-week Dose-Optimization Period followed by a 3-week Dose-Maintenance Period), and a 1-week Washout and Follow-up Period. During the Dose Optimization Period, subjects were titrated until an optimal dose, based on tolerability and investigator’s judgment, was reached. Lisdexamfetamine dimesylate capsules showed significantly greater efficacy than placebo. The placebo-adjusted mean reduction from baseline in the ADHD-RS-IV total score was 18.6. Subjects on lisdexamfetamine dimesylate capsules also showed greater improvement on the Clinical Global Impression-Improvement (CGI-I) rating scale compared to subjects on placebo (Study 5 in Table 6).

Pediatric Patients Ages 6 to 17 Years: Maintenance Treatment in ADHD

Maintenance of Efficacy Study (Study 6) - A double-blind, placebo-controlled, randomized withdrawal study was conducted in pediatric patients ages 6 to 17 years (N=276) who met the diagnosis of ADHD (DSM-IV criteria). A total of 276 patients were enrolled into the study, 236 patients participated in Study 5 and 40 subjects directly enrolled. Subjects were treated with open-label lisdexamfetamine dimesylate capsules for at least 26 weeks prior to being assessed for entry into the randomized withdrawal period. Eligible patients had to demonstrate treatment response as defined by CGI-S <3 and Total Score on the ADHD-RS ≤22. Patients that maintained treatment response for 2 weeks at the end of the open label treatment period were eligible to be randomized to ongoing treatment with the same dose of lisdexamfetamine dimesylate capsules (N=78) or switched to placebo (N=79) during the double-blind phase. Patients were observed

for relapse (treatment failure) during the 6 week double blind phase. A significantly lower proportion of treatment failures occurred among lisdexamfetamine dimesylate capsules subjects (15.8%) compared to placebo (67.5%) at endpoint of the randomized withdrawal period. The endpoint measurement was defined as the last post-randomization treatment week at which a valid ADHD-RS Total Score and CGI-S were observed. Treatment failure was defined as a ≥50% increase (worsening) in the ADHD-RS Total Score and a ≥2-point increase in the CGI-S score compared to scores at entry into the double- blind randomized withdrawal phase. Subjects who withdrew from the randomized withdrawal period and who did not provide efficacy data at their last on-treatment visit were classified as treatment failures (Study 6, Figure 5).

Adults: Short-Term Treatment in ADHD

A double-blind, randomized, placebo-controlled, parallel-group study (Study 7) was conducted in adults ages 18 to 55 (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 lisdexamfetamine dimesylate capsules or placebo for a total of four weeks of treatment. All patients receiving lisdexamfetamine dimesylate capsules were initiated on 30 mg for the first week of treatment. Patients 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). Endpoint was defined as the last post-randomization treatment week (i.e., Weeks 1 through 4) for which a valid score was obtained. All lisdexamfetamine dimesylate capsules dose groups were superior to placebo in the primary efficacy outcome (Study 7 in Table 6).

The second study was a multi-center, randomized, double-blind, placebo-controlled, cross-over, modified analog classroom study (Study 8) of lisdexamfetamine dimesylate capsules to simulate a workplace environment in 142 adults ages 18 to 55 who met DSM-IV-TR criteria for ADHD. There was a 4-week open- label, dose optimization phase with lisdexamfetamine dimesylate capsules (30 mg/day, 50 mg/day, or 70 mg/day in the morning). Patients were then randomized to one of two treatment sequences: 1) lisdexamfetamine dimesylate capsules (optimized dose) followed by placebo, each for one week, or 2) placebo followed by lisdexamfetamine dimesylate capsules, each for one week. Efficacy assessments occurred at the end of each week, using the Permanent Product Measure of Performance (PERMP), a skill-adjusted math test that measures attention in ADHD. PERMP total score results from the sum of the number of math problems attempted plus the number of math problems answered correctly. Lisdexamfetamine dimesylate capsules 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 (Study 8 in Table 6, Figure 6).

Adults: Maintenance Treatment in ADHD

A double-blind, placebo-controlled, randomized withdrawal design study (Study 9) was conducted in adults ages 18 to 55 (N=123) who had a documented diagnosis of ADHD or met DSM-IV criteria for ADHD. At study entry, patients must have had documentation of treatment with lisdexamfetamine dimesylate capsules for a minimum of 6 months and had to demonstrate treatment response as defined by Clinical Global Impression Severity

(CGI-S) ≤3 and Total Score on the ADHD-RS <22. ADHD-RS Total Score is a measure of core symptoms of ADHD. The CGI-S score assesses the clinician's impression of the patient's current illness state and ranges from 1 (not at all ill) to 7 (extremely ill). Patients that maintained treatment response at Week 3 of the open label treatment phase (N=116) were eligible to be randomized to ongoing treatment with the same dose of lisdexamfetamine dimesylate capsules (N=56) or switched to placebo (N=60) during the double-blind phase. Patients were observed for relapse (treatment failure) during the 6-week double-blind phase. The efficacy endpoint was the proportion of patients with treatment failure during the double-blind phase. Treatment failure was defined as a ≥50% increase (worsening) in the ADHD-RS Total Score and ≥2-point increase in the CGI-S score compared to scores at entry into the double-blind phase. Maintenance of efficacy for patients treated with lisdexamfetamine dimesylate capsules was demonstrated by the significantly lower proportion of patients with treatment failure (9%) compared to patients receiving placebo (75%) at endpoint during the double-blind phase (Study 9, Figure 7).

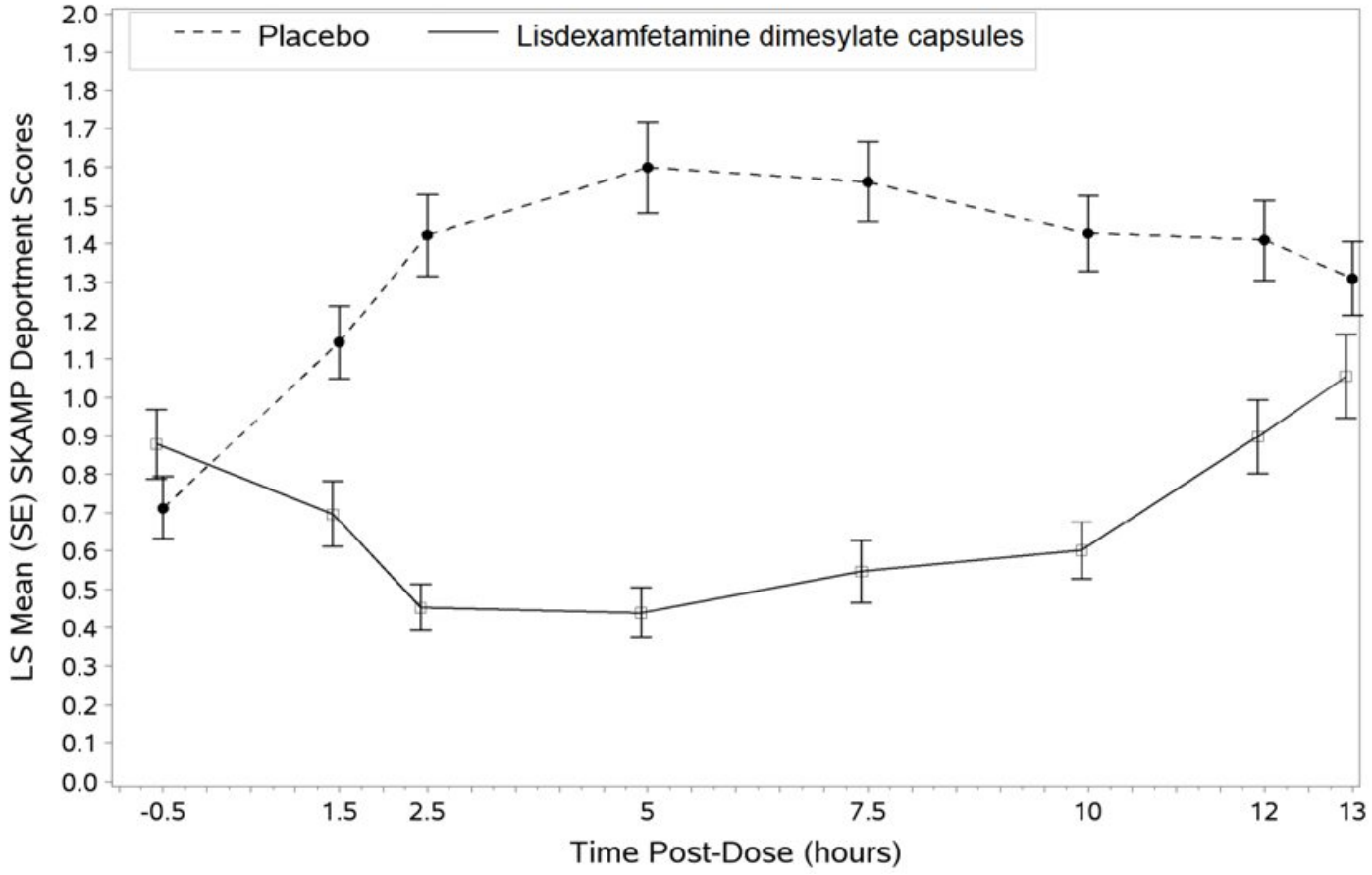
Table 6: Summary of Primary Efficacy Results from Short-term Studies of Lisdexamfetamine Dimesylate Capsules in Pediatric Patients (Ages 6 to 17) and Adults with ADHD

Study Number (Age range)	Primary Endpoint	Treatment Group	Mean Baseline Score (SD)	LS Mean Change from Baseline (SE)	Placebo-subtracted Difference[a] (95% CI)
Study 1 (6 -12 years)	ADHD-RS-IV	Lisdexamfetamine dimesylate capsules (30 mg/day) *	43.2 (6.7)	-21.8 (1.6)	-15.6 (-19.9, -11.2)
		Lisdexamfetamine dimesylate capsules (50 mg/day) *	43.3 (6.7)	-23.4 (1.6)	-17.2 (-21.5, -12.9)
		Lisdexamfetamine dimesylate capsules (70 mg/day) *	45.1(6.8)	-26.7 (1.5)	-20.5 (-24.8, -16.2)
		Placebo	42.4 (7.1)	-6.2 (1.6)	--
Study 2 (6 -12 years)	Average SKAMP-DS	Lisdexamfetamine dimesylate capsules (30, 50 or 70 mg/day) *	--[b]	0.8 (0.1) [d]	-0.9 (-1.1, -0.7)
		Placebo	--[b]	1.7 (0.1) [d]	--
Study 3 (6 -12 years)		Lisdexamfetamine dimesylate capsules (30, 50 or 70 mg/day) *	0.9 (1.0) [c]	0.7 (0.1) [d]	-0.7 (-0.9, -0.6)
		Placebo	0.7 (0.9) [c]	1.4 (0.1) [d]	--
Study 4 (13 -17	ADHD-RS-IV	Lisdexamfetamine dimesylate	38.3 (6.7)	-18.3 (1.2)	-5.5 (-9.0, -2.0)

years)		capsules (30 mg/day) *			
		Lisdexamfetamine dimesylate capsules (50 mg/day) *	37.3 (6.3)	-21.1 (1.3)	-8.3 (-11.8, -4.8)
		Lisdexamfetamine dimesylate capsules (70 mg/day) *	37.0 (7.3)	-20.7 (1.3)	-7.9 (-11.4, -4.5)
		Placebo	38.5 (7.1)	-12.8 (1.2)	--
Study 5 (6 -17 years)	ADHD-RS-IV	Lisdexamfetamine dimesylate capsules (30, 50 or 70 mg/day) *	40.7 (7.3)	-24.3 (1.2)	-18.6 (-21.5, -15.7)
		Placebo	41.0 (7.1)	-5.7 (1.1)	--
Study 7 (18 -55 years)	ADHD-RS-IV	Lisdexamfetamine dimesylate capsules (30 mg/day) *	40.5 (6.2)	-16.2 (1.1)	-8.0 (-11.5, -4.6)
		Lisdexamfetamine dimesylate capsules (50 mg/day) *	40.8 (7.3)	-17.4 (1.0)	-9.2 (-12.6, -5.7)
		Lisdexamfetamine dimesylate capsules (70 mg/day) *	41.0 (6.0)	-18.6 (1.0)	-10.4 (-13.9, -6.9)
		Placebo	39.4 (6.4)	-8.2 (1.4)	
Study 8 (18 -55 years)	Average PERMP	Lisdexamfetamine dimesylate capsules (30, 50 or 70 mg/day) *	260.1 (86.2) [c]	312.9 (8.6) [d]	23.4 (15.6, 31.2)
		Placebo	261.4 (75.0) [c]	289.5 (8.6) [d]	

SD: standard deviation; SE: standard error; LS Mean: least-squares mean; CI: confidence interval.
[a] Difference (drug minus placebo) in least-squares mean change from baseline.
[b] Pre-dose SKAMP-DS was not collected.
[c] Pre-dose SKAMP-DS (Study 3) or PERMP (Study 8) total score, averaged over both periods.
[d] LS Mean for SKAMP-DS (Study 2 and 3) or PERMP (Study 8) is post-dose average score over all sessions of the treatment day, rather than change from baseline.
* Doses statistically significantly superior to placebo.

Figure 4 LS Mean SKAMP Deportment Subscale Score by Treatment and Time-point for Pediatric Patients Ages 6 to 12 with ADHD after 1 Week of Double Blind Treatment (Study 3)



Higher score on the SKAMP-Deportment scale indicates more severe symptoms

Figure 5 Kaplan-Meier Estimated Proportion of Patients with Treatment Failure for Pediatric Patients Ages 6 to 17 (Study 6)

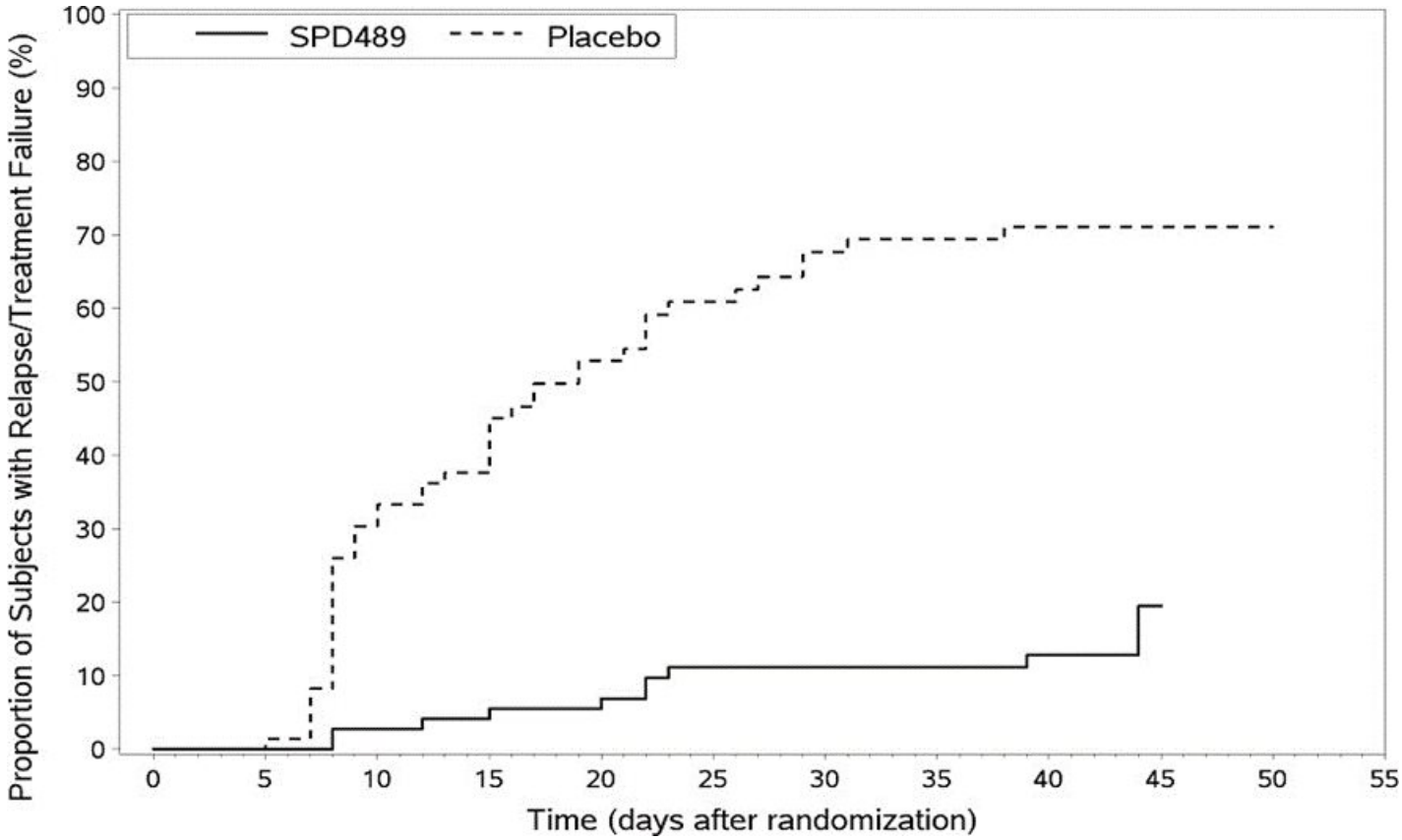
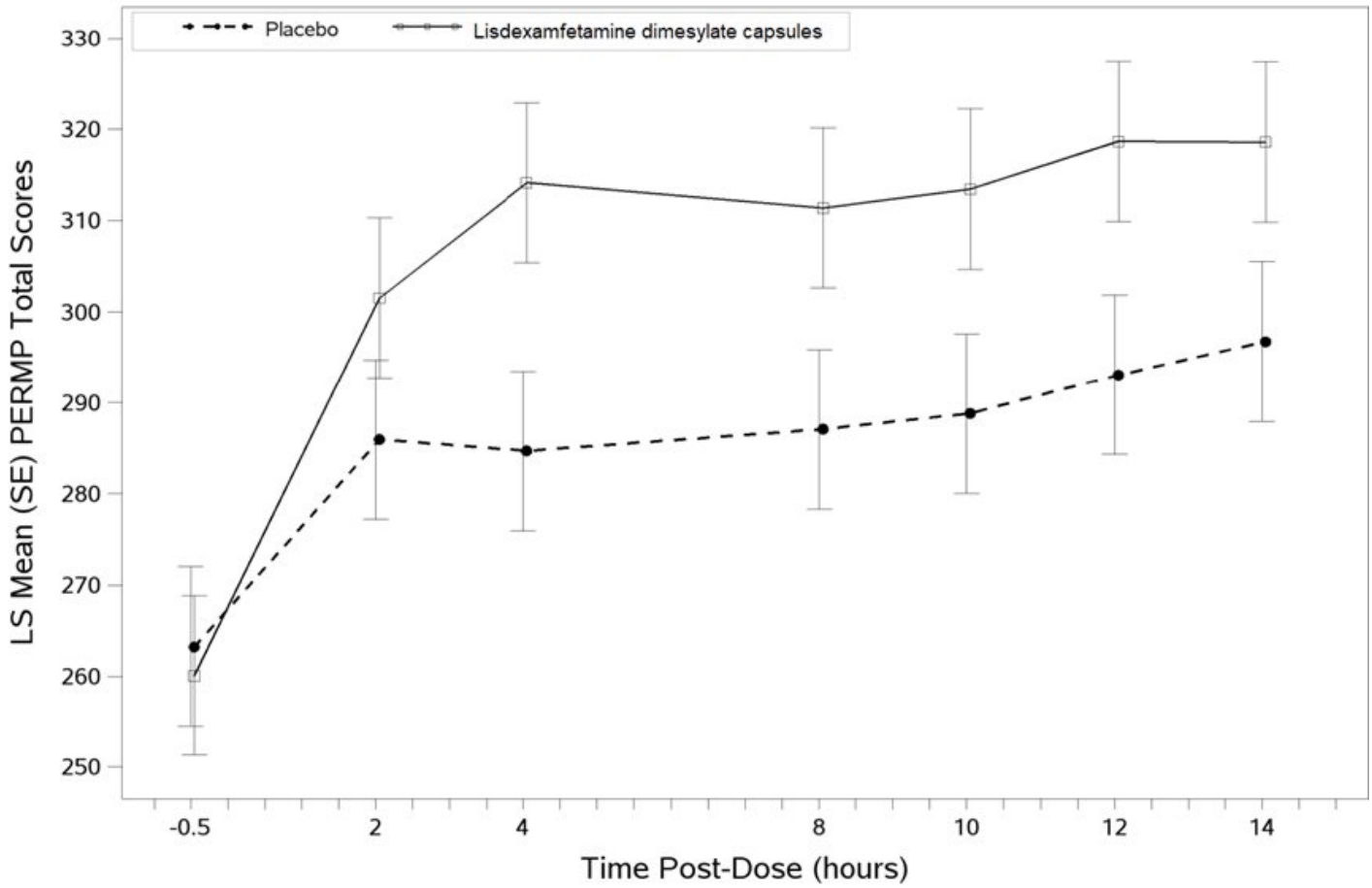
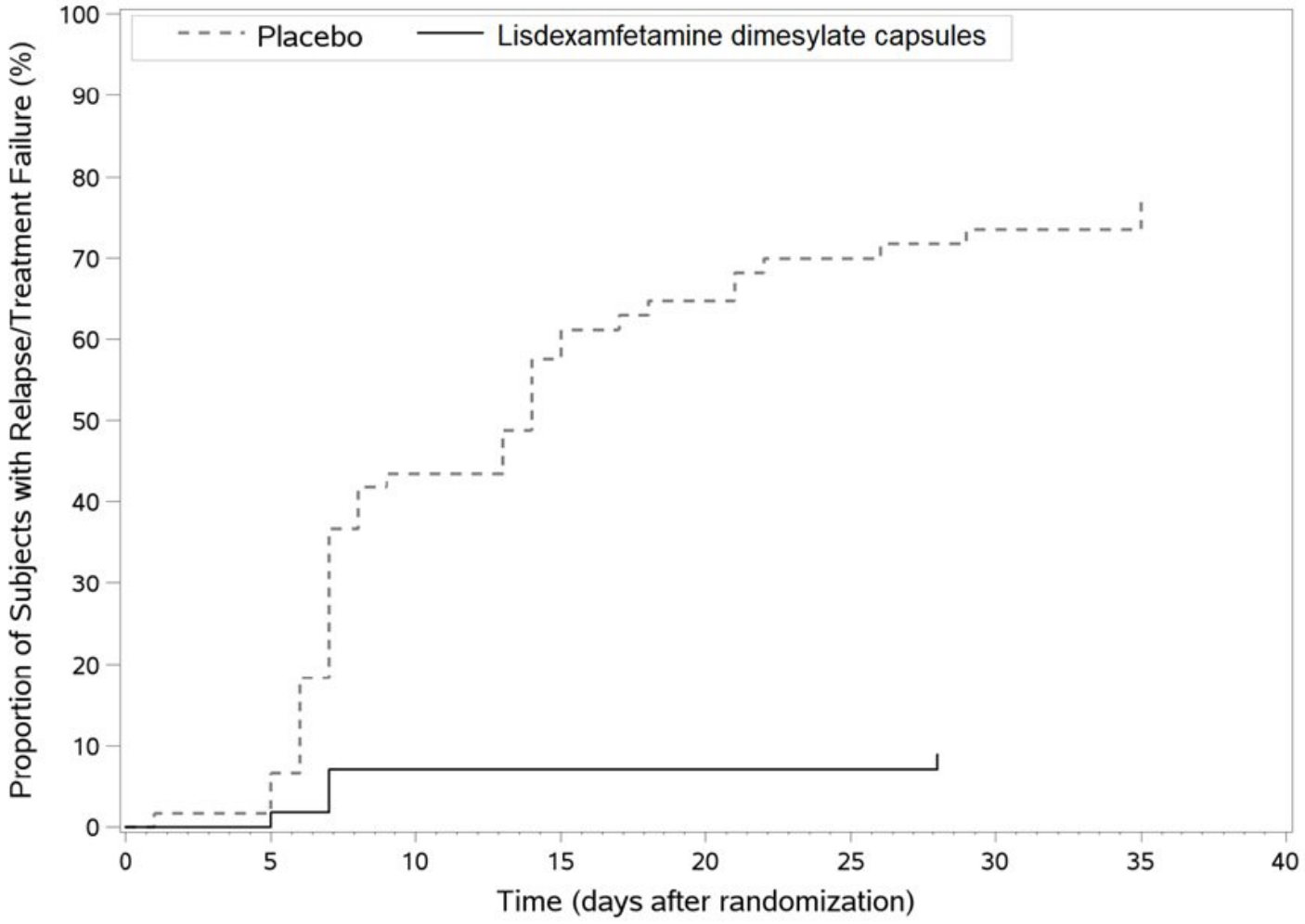


Figure 6 LS Mean (SE) PERMP Total Score by Treatment and Time-point for Adults Ages 18 to 55 with ADHD after 1 Week of Double Blind Treatment (Study 8)



Higher score on the PERMP scale indicates less severe symptoms.

Figure 7 Kaplan-Meier Estimated Proportion of Subjects with Relapse in Adults with ADHD (Study 9)



14.2 Binge Eating Disorder (BED)

A phase 2 study evaluated the efficacy of lisdexamfetamine dimesylate capsules 30, 50 and 70 mg/day compared to placebo in reducing the number of binge days/week in adults with at least moderate to severe BED. This randomized, double-blind, parallel-group, placebo-controlled, forced-dose titration study (Study 10) consisted of an 11-week double-blind treatment period (3 weeks of forced-dose titration followed by 8 weeks of dose maintenance). Lisdexamfetamine dimesylate capsules 30 mg/day was not statistically different from placebo on the primary endpoint. The 50 and 70 mg/day doses were statistically superior to placebo on the primary endpoint.

The efficacy of lisdexamfetamine dimesylate capsules in the treatment of BED was demonstrated in two 12-week randomized, double-blind, multi-center, parallel-group, placebo-controlled, dose-optimization studies (Study 11 and Study 12) in adults aged 18-55 years (Study 11: N=374, Study 12: N=350) with moderate to severe BED. A diagnosis of BED was confirmed using DSM-IV criteria for BED. Severity of BED was determined based on having at least 3 binge days per week for 2 weeks prior to the baseline visit and on having a Clinical Global Impression Severity (CGI-S) score of ≥4 at the baseline visit. For both studies, a binge day was defined as a day with at least 1 binge episode, as determined from the subject’s daily binge diary.

Both 12-week studies consisted of a 4-week dose-optimization period and an 8-week dose- maintenance period. During dose-optimization, subjects assigned to lisdexamfetamine dimesylate capsules began treatment at the titration dose of 30

mg/day and, after 1 week of treatment, were subsequently titrated to 50 mg/day. Additional increases to 70 mg/day were made as tolerated and clinically indicated. Following the dose-optimization period, subjects continued on their optimized dose for the duration of the dose-maintenance period.

The primary efficacy outcome for the two studies was defined as the change from baseline at Week 12 in the number of binge days per week. Baseline is defined as the weekly average of the number of binge days per week for the 14 days prior to the baseline visit. Subjects from both studies on lisdexamfetamine dimesylate capsules had a statistically significantly greater reduction from baseline in mean number of binge days per week at Week 12. In addition, subjects on lisdexamfetamine dimesylate capsules showed greater improvement as compared to placebo across key secondary outcomes with higher proportion of subjects rated improved on the CGI-I rating scale, higher proportion of subjects with 4-week binge cessation, and greater reduction in the Yale-Brown Obsessive Compulsive Scale Modified for Binge Eating (Y-BOCS-BE) total score.

Table 7: Summary of Primary Efficacy Results in BED

Study Number	**Treatment Group**	**Primary Efficacy Measure: Binge Days per Week at Week 12**		
		Mean Baseline Score (SD)	**LS Mean Change from Baseline (SE)**	**Placebo-subtracted Difference [a] (95% CI)**
Study 11	Lisdexamfetamine dimesylate capsules (50 or 70 mg/day)*	4.79(1.27)	-3.87 (0.12)	-1.35 (-1.70, -1.01)
	Placebo	4.60 (1.21)	-2.51 (0.13)	--
Study 12	Lisdexamfetamine dimesylate capsules (50 or 70 mg/day)*	4.66 (1.27)	-3.92 (0.14)	-1.66 (-2.04, -1.28)
	Placebo	4.82 (1.42)	-2.26 (0.14)	

SD: standard deviation; SE: standard error; LS Mean: least-squares mean; CI: confidence interval.

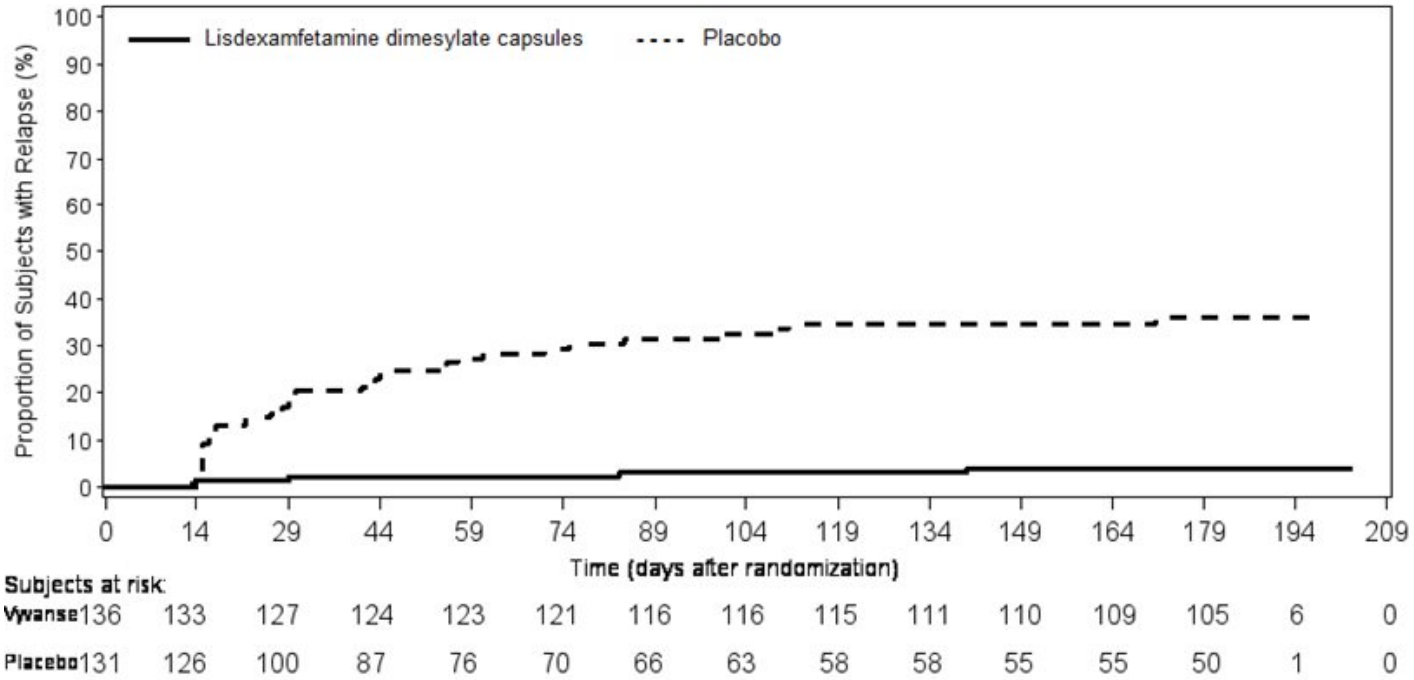
[a] Difference (drug minus placebo) in least-squares mean change from baseline.

* Doses statistically significantly superior to placebo.

A double-blind, placebo controlled, randomized withdrawal design study (Study 13) was conducted to evaluate maintenance of efficacy based on time to relapse between lisdexamfetamine dimesylate capsules and placebo in adults aged 18 to 55 (N=267) with moderate to severe BED. In this longer-term study patients who had responded to lisdexamfetamine dimesylate capsules in the preceding 12-week open-label treatment phase were randomized to continuation of lisdexamfetamine dimesylate capsules or placebo for up to 26 weeks of observation for relapse. Response in the open-label phase was defined as 1 or fewer binge days each week for four consecutive weeks prior to the last visit at the end of the 12-week open-label phase and a CGI-S score of 2 or less at the same visit. Relapse during the double-blind phase was defined as having 2 or more binge days each week for two consecutive weeks (14 days) prior to any visit and having an increase in CGI-S score of 2 or more points compared to the randomized- withdrawal

baseline. Maintenance of efficacy for patients who had an initial response during the open-label period and then continued on lisdexamfetamine dimesylate capsules during the 26-week double-blind randomized-withdrawal phase was demonstrated with lisdexamfetamine dimesylate capsules being superior over placebo as measured by time to relapse.

Figure 8 Kaplan-Meier Estimated Proportions of Subjects with Relapse in Adults with BED (Study 13)



Examination of population subgroups based on age (there were no patients over 65), gender, and race did not reveal any clear evidence of differential responsiveness in the treatment of BED.

16 HOW SUPPLIED/STORAGE AND HANDLING

Click here to enter How Supplied

16.1 How Supplied

Lisdexamfetamine dimesylate capsules:

- Lisdexamfetamine dimesylate capsules 10 mg: SIZE "3" Capsule, opaque pink body/opaque pink cap (imprinted with S6 10), bottles of 100, NDC 43547-602-10
- Lisdexamfetamine dimesylate capsules 20 mg: SIZE “3” Capsule, opaque ivory body/opaque ivory cap (imprinted with S6 20), bottles of 100, NDC 43547-603-10
- Lisdexamfetamine dimesylate capsules 30 mg: SIZE “3” Capsule, opaque white body/opaque orange cap (imprinted with S6 30), bottles of 100, NDC 43547-604-10

- Lisdexamfetamine dimesylate capsules 40 mg: SIZE “3” Capsule, opaque white body/opaque blue green cap (imprinted with S6 40), bottles of 100, NDC 43547-605-10
- Lisdexamfetamine dimesylate capsules 50 mg: SIZE “3” Capsule, opaque white body/opaque blue cap (imprinted with S6 50), bottles of 100, NDC 43547-606-10
- Lisdexamfetamine dimesylate capsules 60 mg: SIZE “3” Capsule, opaque aqua blue body/opaque aqua blue cap (imprinted with S6 60), bottles of 100, NDC 43547-607-10
- Lisdexamfetamine dimesylate capsules 70 mg: SIZE “3” Capsule, opaque blue body/opaque orange cap (imprinted with S6 70), bottles of 100, NDC 43547-608-10

16.2 Storage and Handling

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

Store at room temperature, 20ºC to 25ºC (68ºF to 77ºF). Excursions permitted between 15ºC and 30ºC (59 to 86ºF) *[see USP Controlled Room Temperature]*.

Disposal

Comply with local laws and regulations on drug disposal of CNS stimulants. Dispose of remaining, unused, or expired lisdexamfetamine dimesylate capsules by a medicine take-back program.

17 PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Medication Guide).

Controlled Substance Status/High Potential for Abuse and Dependence

Advise patients that lisdexamfetamine dimesylate capsule is a controlled substance and it can be abused and lead to dependence and not to give lisdexamfetamine dimesylate capsules to anyone else *[see Drug Abuse and Dependence (9.1, 9.2, and 9.3)]*. Advise patients to store lisdexamfetamine dimesylate capsules in a safe place, preferably locked, to prevent abuse. Advise patients to dispose of remaining, unused, or expired lisdexamfetamine dimesylate capsules by a medicine take-back program.

Serious Cardiovascular Risks

Advise patients that there is a potential serious cardiovascular risk including sudden death, myocardial infarction, stroke, and hypertension with lisdexamfetamine dimesylate capsules use. Instruct patients to contact a healthcare provider immediately if they develop symptoms such as exertional chest pain, unexplained syncope, or other symptoms suggestive of cardiac disease *[see Warnings and Precautions (5.2)]*.

Hypertension and Tachycardia

Instruct patients that lisdexamfetamine dimesylate capsules can cause elevations of their blood pressure and pulse rate and they should be monitored for such effects.

Psychiatric Risks

Advise patients that lisdexamfetamine dimesylate capsules at recommended doses may cause psychotic or manic symptoms even in patients without prior history of psychotic symptoms or mania *[see Warnings and Precautions (5.4)]*.

Suppression of Growth

Advise patients that lisdexamfetamine dimesylate capsules may cause slowing of growth including weight loss *[see Warnings and Precautions (5.5)]*.

Impairment in Ability to Operate Machinery or Vehicles

Advise patients that lisdexamfetamine dimesylate capsules may impair their ability to engage in potentially dangerous activities such as operating machinery or vehicles. Instruct patients to find out how lisdexamfetamine dimesylate capsules will affect them before engaging in potentially dangerous activities *[see Adverse Reactions (6.1, 6.2)]*.

Circulation problems in fingers and toes [Peripheral vasculopathy, including Raynaud'sphenomenon]

Instruct patients beginning treatment with lisdexamfetamine dimesylate capsules about the risk of peripheral vasculopathy, including Raynaud's phenomenon, and associated signs and symptoms: fingers or toes may feel numb, cool, painful, and/or may change from pale, to blue, to red. Instruct patients to report to their physician any new numbness, pain, skin color change, or sensitivity to temperature in fingers or toes. Instruct patients to call their physician immediately with any signs of unexplained wounds appearing on fingers or toes while taking lisdexamfetamine dimesylate capsules. Further clinical evaluation (e.g., rheumatology referral) may be appropriate for certain patients *[see Warnings and Precautions (5.6)]*.

Serotonin Syndrome

Caution patients about the risk of serotonin syndrome with concomitant use of lisdexamfetamine dimesylate capsules and other serotonergic drugs including SSRIs, SNRIs, triptans, tricyclic antidepressants, fentanyl, lithium, tramadol, tryptophan, buspirone, St. John's Wort, and with drugs that impair metabolism of serotonin (in particular MAOIs, both those intended to treat psychiatric disorders and also others such as linezolid *[see Contraindications (4), Warnings and Precautions (5.7) and Drug Interactions (7.1)]*. Advise patients to contact their healthcare provider or report to the emergency room if they experience signs or symptoms of serotonin syndrome.

Concomitant Medications

Advise patients to notify their physicians if they are taking, or plan to take, any prescription or over-the-counter drugs because there is a potential for interactions *[see Drug Interactions (7.1)]*.

Pregnancy

Advise patients of the potential fetal effects from the use of lisdexamfetamine dimesylate capsules during pregnancy. Advise patients to notify their healthcare provider if they become pregnant or intend to become pregnant during treatment with lisdexamfetamine dimesylate capsules *[see Use in Specific Populations (8.1)]*.

Lactation

Advise women not to breastfeed if they are taking lisdexamfetamine dimesylate capsules *[see Use in Specific Populations (8.2)]*.

Administration Instructions

Capsules: Advise patients to take the capsules whole or empty and mix the entire

contents with yogurt, water, or orange juice. Advise patients to consume the mixture immediately and not to store for future use *[see Dosage and Administration (2.2)].*

Dispense with Medication Guide available at:

www.solcohealthcare.com/medguide/lisdexamfetamine-dimesylate-capsules.pdf

Manufactured by: Prinston Laboratories

Charlotte, NC 28206, USA

Distributed by: Solco Healthcare US, LLC

Somerset, NJ 08873, USA

For more information call 1-866-257-2597

Revised: 03/2023

9040614-01

Medication Guide

Dispense with Medication Guide available at:

www.solcohealthcare.com/medguide/lisdexamfetamine-dimesylate-capsules.pdf

Lisdexamfetamine Dimesylate Capsules

(lis dex″ am fet′ a meen dye mes′ i late) CII

What is the most important information I should know about lisdexamfetamine dimesylate capsules?

Lisdexamfetamine dimesylate capsules may cause serious side effects, including:

- **Abuse and dependence.** Lisdexamfetamine dimesylate capsules, other amphetamine containing medicines, and methylphenidate have a high chance for abuse and may cause physical and psychological dependence. Your healthcare provider should check you or your child for signs of abuse and dependence before and during treatment with lisdexamfetamine dimesylate capsules.
- Tell your healthcare provider if you or your child have ever abused or been dependent on alcohol, prescription medicines, or street drugs.
- Your healthcare provider can tell you more about the differences between physical and psychological dependence and drug addiction.
- **Heart-related problems including:**
- sudden death, stroke, and heart attack in adults
- sudden death in children who have heart problems or heart defects
- increased blood pressure and heart rate
  Your healthcare provider should check you or your child carefully for heart problems before starting treatment with lisdexamfetamine dimesylate capsules. Tell your healthcare provider if you or your child have any heart problems, heart defects, high blood pressure, or a family history of these problems.
  Your healthcare provider should check your or your child’s blood pressure and heart rate regularly during treatment with lisdexamfetamine dimesylate capsules.

Call your healthcare provider or go to the nearest hospital emergency room right away if you or your child have any signs of heart problems such as chest pain, shortness of breath, or fainting during treatment with lisdexamfetamine dimesylate capsules.

- **Mental (psychiatric) problems, including:**
- new or worse behavior and thought problems
- new or worse bipolar illness
- new psychotic symptoms (such as hearing voices, or seeing or believing things that are not real) or new manic symptoms

  Tell your healthcare provider about any mental problems you or your child have or about a family history of suicide, bipolar illness, or depression.

  Call your healthcare provider right away if you or your child have any new or worsening mental symptoms or problems during treatment with lisdexamfetamine dimesylate capsules, especially hearing voices, seeing or believing things that are not real, or new manic symptoms.

What are lisdexamfetamine dimesylate capsules?

Lisdexamfetamine dimesylate is a central nervous system (CNS) stimulant prescription medicine used for the treatment of:

- Attention Deficit Hyperactivity Disorder (ADHD) in adults and children 6 years of age and older. Lisdexamfetamine dimesylate capsules may help increase attention and decrease impulsiveness and hyperactivity in people with ADHD.
- Moderate to severe binge eating disorder (BED) in adults. Lisdexamfetamine dimesylate capsules may help reduce the number of binge eating days in people with BED.

Lisdexamfetamine dimesylate capsules are not for use in children under 6 years of age with ADHD.

Lisdexamfetamine dimesylate capsules are not for weight loss. It is not known if Lisdexamfetamine dimesylate capsules are safe and effective for the treatment of obesity.

It is not known if lisdexamfetamine dimesylate capsules are safe and effective for use in children with BED.

Lisdexamfetamine dimesylate capsule is a federally controlled substance (CII) because it contains lisdexamfetamine dimesylate that can be a target for people who abuse prescription medicines or street drugs. Keep lisdexamfetamine dimesylate capsules in a safe place to protect it from theft. Never give your lisdexamfetamine dimesylate capsules to anyone else because it may cause death or harm them. Selling or giving away lisdexamfetamine dimesylate capsules may harm others and is against the law.

Do not take lisdexamfetamine dimesylate capsules if your child are:

- allergic to amphetamine products or any of the ingredients in lisdexamfetamine dimesylate capsules. See the end of this Medication Guide for a complete list of ingredients in lisdexamfetamine dimesylate capsules.
- taking, or have stopped taking in the last 14 days, a medicine called a Monoamine Oxidase Inhibitor (MAOI).

- being treated with the antibiotic linezolid or intravenous methylene blue.

Before taking lisdexamfetamine dimesylate capsules, tell your healthcare provider about all medical conditions, including if you or your child:

- have heart problems, heart defects, or high blood pressure
- have mental problems including psychosis, mania, bipolar illness, or depression or have a family history of suicide, bipolar illness, or depression
- have circulation problems in fingers and toes
- are pregnant or plan to become pregnant. Lisdexamfetamine dimesylate capsules may harm the unborn baby.
- There is a pregnancy registry for females who are exposed to lisdexamfetamine dimesylate capsules during pregnancy. The purpose of the registry is to collect information about the health of females exposed to lisdexamfetamine dimesylate capsules and their baby. If you or your child becomes pregnant during treatment with lisdexamfetamine dimesylate capsules, talk to your healthcare provider about registering with the National Pregnancy Registry for Psychostimulants at 1-866-961-2388 or visit online at https://womensmentalhealth.org/research/pregnancyregistry/adhd-medications/.
- are breastfeeding or plan to breastfeed. Lisdexamfetamine dimesylate passes into breast milk. You should not breastfeed during treatment with lisdexamfetamine dimesylate capsules. Talk to your healthcare provider about the best way to feed the baby during treatment with lisdexamfetamine dimesylate capsules.

Tell your healthcare provider about all the medicines that you or your child take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

Lisdexamfetamine dimesylate capsules can affect the way other medicines work and other medicines may affect how lisdexamfetamine dimesylate capsules work. Taking lisdexamfetamine dimesylate capsules with other medicines can cause serious side effects. Sometimes the doses of other medicines will need to be changed while taking lisdexamfetamine dimesylate capsules.

Especially tell your healthcare provider if you or your child take:

- selective serotonin reuptake inhibitors (SSRIs)
- serotonin norepinephrine reuptake inhibitors (SNRIs)
- medicines used to treat migraine headaches called triptans
- tricyclic antidepressants
- lithium
- fentanyl
- tramadol
- tryptophan
- buspirone
- St. John’s Wort

Keep a list of all medicines to show your healthcare provider and pharmacist when you get a new medicine. Your healthcare provider will decide if lisdexamfetamine dimesylate capsules can be taken with other medicines.

Do not start any new medicine during treatment with lisdexamfetamine dimesylate capsules without talking to your healthcare provider first.

How should lisdexamfetamine dimesylate capsules be taken?

- Take lisdexamfetamine dimesylate capsules exactly as prescribed by your healthcare provider.
- Your healthcare provider may change the dose if needed.
- Take lisdexamfetamine dimesylate capsules 1 time each day in the morning with or without food.
- Your healthcare provider may sometimes stop lisdexamfetamine dimesylate capsules treatment for a while to check ADHD or BED symptoms.
- Lisdexamfetamine dimesylate comes in capsules.
  Taking Lisdexamfetamine Dimesylate Capsules:
- Lisdexamfetamine dimesylate capsules may be swallowed whole.
- If lisdexamfetamine dimesylate capsules cannot be swallowed whole, the capsule may be opened and the entire contents sprinkled onto yogurt, or poured into water or orange juice.
- Using a spoon, break apart any powder that is stuck together. Stir the lisdexamfetamine dimesylate capsules powder and yogurt, water, or orange juice until they are completely mixed together.
- Swallow all the yogurt, water, or orange juice mixture right away. **Do not** store the yogurt, water, or orange juice mixture.
- It is normal to see a filmy coating on the inside of your glass or container after you eat or drink all the lisdexamfetamine dimesylate capsules mixture.

If you or your child take too many lisdexamfetamine dimesylate capsules, call your healthcare provider or poison control center at 1-800-222-1222 or go to the nearest hospital emergency room right away.

What should I avoid while taking lisdexamfetamine dimesylate capsules?

Do not drive, operate machinery, or do other dangerous activities until you know how lisdexamfetamine dimesylate capsules affect you.

What are the possible side effects of lisdexamfetamine dimesylate capsules? Lisdexamfetamine dimesylate capsules may cause serious side effects, including:

- See **“What is the most important information I should know about lisdexamfetamine dimesylate capsules?”**
- **Slowing of growth (height and weight) in children.** Children should have their height and weight checked often during treatment with lisdexamfetamine dimesylate capsules. Lisdexamfetamine dimesylate capsules treatment may be stopped if your child is not growing or gaining weight.
- **Circulation problems in fingers and toes (Peripheral vasculopathy, including Raynaud’s phenomenon).** Signs and symptoms may include:

- Fingers or toes may feel numb, cool, painful
- Fingers or toes may change color from pale, to blue, to red
  Tell your healthcare provider if you or your child have numbness, pain, skin color change, or sensitivity to temperature in your fingers or toes.
  Call your healthcare provider right away if you or your child have any signs of unexplained wounds appearing on fingers or toes during treatment with lisdexamfetamine dimesylate capsules.
- **Serotonin Syndrome.** A potentially life-threatening problem called serotonin syndrome may happen when lisdexamfetamine dimesylate capsules are taken with certain other medicines. Stop taking lisdexamfetamine dimesylate capsules and call your healthcare provider or go to the nearest hospital emergency room right away if you or your child develop any of the following signs and symptoms of serotonin syndrome:

- agitation
- flushing
- coma
- loss of coordination
- dizziness
- seeing or hearing things that are not real (hallucination)
- high body temperature (hyperthermia)
- fast heartbeat
- seizures
- sweating
- confusion
- tremors, stiff muscles, or muscle twitching
- changes in blood pressure
- nausea, vomiting, diarrhea

The most common side effects of lisdexamfetamine dimesylate capsules in children 6 to 17 years old and adults with ADHD include:

- loss of appetite (anorexia)
- decreased appetite
- diarrhea
- anxiety
- weight loss
- dizziness

- dry mouth
- trouble sleeping
- stomach pain
- irritability
- nausea
- vomiting

The most common side effects of lisdexamfetamine dimesylate capsules in adults with BED include:

- dry mouth
- decreased appetite
- constipation
- anxiety
- trouble sleeping
- increased heart rate
- feeling jittery

These are not all the possible side effects of lisdexamfetamine dimesylate capsules. Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How should I store lisdexamfetamine dimesylate capsules?

- Store lisdexamfetamine dimesylate capsules in a safe place (like a locked cabinet) and in a tightly closed container at room temperature between 68°F to 77°F (20°C to 25°C).
- Protect lisdexamfetamine dimesylate capsules from light.
- Dispose of remaining, unused, or expired lisdexamfetamine dimesylate capsules by a medicine take-back program at authorized collection sites such as retail pharmacies, hospital or clinic pharmacies, and law enforcement locations. If no take-back program or authorized collector is available, mix lisdexamfetamine dimesylate capsules with an undesirable, nontoxic substance such as dirt, cat litter, or used coffee grounds to make it less appealing to children and pets. Place the mixture in a container such as a sealed plastic bag and throw away (discard) lisdexamfetamine dimesylate capsules in the household trash.

Keep lisdexamfetamine dimesylate capsules and all medicines out of the reach of children.

General information about the safe and effective use of lisdexamfetamine dimesylate capsules.

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. Do not use lisdexamfetamine dimesylate capsules for a condition for which it was

not prescribed. Do not give lisdexamfetamine dimesylate capsules to other people, even if they have the same symptoms that you have. It may harm them and it is against the law. You can ask your pharmacist or healthcare provider for information about lisdexamfetamine dimesylate capsules that is written for health professionals.

What are the ingredients in lisdexamfetamine dimesylate capsules?

Active ingredient: lisdexamfetamine dimesylate

Capsule Inactive ingredients: croscarmellose sodium, microcrystalline cellulose, and magnesium stearate.

The imprinting ink for all strengths contain D&C yellow #10 Aluminum Lake, FD&C Blue #1 Aluminum Lake, FD&C Blue #2 Aluminum Lake, FD&C Red #40 Aluminum Lake, iron oxide black, potassium hydroxide, propylene glycol and shellac glaze.

The capsule shells of each strength contain ingredients as below:

Strength	**Ingredients**
10 mg	FD&C Blue 1, FD&C Red 3, gelatin, titanium dioxide and sodium lauryl sulfate
20 mg	Iron Oxide Yellow, gelatin, titanium dioxide and sodium lauryl sulfate
30 mg	FD&C Red 3, FD&C Yellow 6, gelatin, titanium dioxide and sodium lauryl sulfate
40 mg	FD&C Blue 1, Iron Oxide Black, Iron Oxide Yellow, gelatin, titanium dioxide and sodium lauryl sulfate
50 mg	FD&C Blue 1, gelatin, titanium dioxide and sodium lauryl sulfate
60 mg	FD&C Blue 1, gelatin, titanium dioxide and sodium lauryl sulfate
70 mg	FD&C Blue 1, FD&C Red 3, FD&C Yellow 6, gelatin, titanium dioxide and sodium lauryl sulfate

Manufactured by: Prinston Laboratories

Charlotte, NC 28206, USA

Distributed by: Solco Healthcare US, LLC

Somerset, NJ 08873, USA

For more information call 1-866-257-2597.

This Medication Guide has been approved by the U.S. Food and Drug Administration.

Revised: 03/2023

PACKAGE/LABEL PRINCIPAL DISPLAY PANEL

Lisdexamfetamine Dimesylate Capsules

NDC 43547-602-10

SEE PACKAGE INSERT FOR DOSAGE INFORMATION

Each capsule contains: Lisdexamfetamine dimesylate 10 mg (equivalent to 5.8 mg lisdexamfetamine)

Store at room temperature, 20ºC to 25º C (68ºF to 77º F). Excursions permitted between 15ºC and 30º C (59º F to 86º F): dispense in a tight, light-resistant container as defined in the USP.

Manufactured by:

Prinston Laboratories

Charlotte, NC 28206, USA

Distributed by:

Solco Healthcare US, LLC

Somerset, NJ 08873, USA

9040613-01

02/2023

PACKAGE/LABEL PRINCIPAL DISPLAY PANEL

Lisdexamfetamine Dimesylate Capsules

NDC 43547-603-10

SEE PACKAGE INSERT FOR DOSAGE INFORMATION

Each capsule contains: Lisdexamfetamine dimesylate 20 mg (equivalent to 11.6 mg lisdexamfetamine)

Store at room temperature, 20ºC to 25º C (68ºF to 77º F). Excursions permitted between 15ºC and 30º C (59º F to 86º F): dispense in a tight, light-resistant container as defined in the USP.

Manufactured by:

Prinston Laboratories

Charlotte, NC 28206, USA

Distributed by:

Solco Healthcare US, LLC

Somerset, NJ 08873, USA

9040612-01

02/2023

PACKAGE/LABEL PRINCIPAL DISPLAY PANEL

Lisdexamfetamine Dimesylate Capsules

NDC 43547-604-10

SEE PACKAGE INSERT FOR DOSAGE INFORMATION

Each capsule contains: Lisdexamfetamine dimesylate 30 mg (equivalent to 17.3 mg lisdexamfetamine)

Store at room temperature, 20ºC to 25º C (68ºF to 77º F). Excursions permitted between 15ºC and 30º C (59º F to 86º F): dispense in a tight, light-resistant container as defined in the USP.

Manufactured by:

Prinston Laboratories

Charlotte, NC 28206, USA

Distributed by:

Solco Healthcare US, LLC

Somerset, NJ 08873, USA

9040611-01

02/2023

PACKAGE/LABEL PRINCIPAL DISPLAY PANEL

Lisdexamfetamine Dimesylate Capsules

NDC 43547-605-10

SEE PACKAGE INSERT FOR DOSAGE INFORMATION

Each capsule contains: Lisdexamfetamine dimesylate 40 mg (equivalent to 23.1 mg lisdexamfetamine)

Store at room temperature, 20ºC to 25º C (68ºF to 77º F). Excursions permitted between 15ºC and 30º C (59º F to 86º F): dispense in a tight, light-resistant container as defined in the USP.

Manufactured by:

Prinston Laboratories

Charlotte, NC 28206, USA

Distributed by:

Solco Healthcare US, LLC

Somerset, NJ 08873, USA

9040610-01

02/2023

PACKAGE/LABEL PRINCIPAL DISPLAY PANEL

Lisdexamfetamine Dimesylate Capsules

NDC 43547-606-10

SEE PACKAGE INSERT FOR DOSAGE INFORMATION

Each capsule contains: Lisdexamfetamine dimesylate 50 mg (equivalent to 28.9 mg lisdexamfetamine)

Store at room temperature, 20ºC to 25º C (68ºF to 77º F). Excursions permitted between 15ºC and 30º C (59º F to 86º F): dispense in a tight, light-resistant container as defined in the USP.

Manufactured by:

Prinston Laboratories

Charlotte, NC 28206, USA

Distributed by:

Solco Healthcare US, LLC

Somerset, NJ 08873, USA

9040609-01

02/2023

Package/Label Display Panel

Lisdexamfetamine Dimesylate Capsules

NDC 43547-607-10

SEE PACKAGE INSERT FOR DOSAGE INFORMATION

Each capsule contains: Lisdexamfetamine dimesylate 60 mg (equivalent to 34.7 mg lisdexamfetamine)

Store at room temperature, 20ºC to 25º C (68ºF to 77º F). Excursions permitted between 15ºC and 30º C (59º F to 86º F): dispense in a tight, light-resistant container as defined in the USP.

Manufactured by:

Prinston Laboratories

Charlotte, NC 28206, USA

Distributed by:

Solco Healthcare US, LLC

Somerset, NJ 08873, USA

9040608-01

02/2023

PACKAGE/LABEL PRINCIPAL DISPLAY PANEL

Lisdexamfetamine Dimesylate Capsules

NDC 43547-608-10

SEE PACKAGE INSERT FOR DOSAGE INFORMATION

Each capsule contains: Lisdexamfetamine dimesylate 70 mg (equivalent to 40.5 mg lisdexamfetamine)

Store at room temperature, 20ºC to 25º C (68ºF to 77º F). Excursions permitted between 15ºC and 30º C (59º F to 86º F): dispense in a tight, light-resistant container as defined in the USP.

Manufactured by:

Prinston Laboratories

Charlotte, NC 28206, USA

Distributed by:

Solco Healthcare US, LLC

Somerset, NJ 08873, USA

9040607-01

02/2023

LISDEXAMFETAMINE DIMESYLATE

lisdexamfetamine dimesylate capsules capsule

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:43547-602
Route of Administration	ORAL	**DEA Schedule**	CII

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
LISDEXAMFETAMINE DIMESYLATE (UNII: SJT761GEGS) (LISDEXAMFETAMINE - UNII:H645GUL8KJ)	LISDEXAMFETAMINE DIMESYLATE	10 mg

Inactive Ingredients

Ingredient Name	Strength
CROSCARMELLOSE SODIUM (UNII: M28OL1HH48)	
D&C YELLOW NO. 10 ALUMINUM LAKE (UNII: CQ3XH3DET6)	
FD&C BLUE NO. 1 (UNII: H3R47K3TBD)	
FD&C BLUE NO. 1--ALUMINUM LAKE (UNII: J9EQA3S2JM)	
FD&C BLUE NO. 2--ALUMINUM LAKE (UNII: 4AQJ3LG584)	
FD&C RED NO. 3 (UNII: PN2ZH5LOQY)	
FD&C RED NO. 40 (UNII: WZB9127XOA)	
FERROSOFERRIC OXIDE (UNII: XM0M87F357)	
GELATIN, UNSPECIFIED (UNII: 2G86QN327L)	
MAGNESIUM STEARATE (UNII: 70097M6I30)	
MICROCRYSTALLINE CELLULOSE (UNII: OP1R32D61U)	
POTASSIUM HYDROXIDE (UNII: WZH3C48M4T)	
PROPYLENE GLYCOL (UNII: 6DC9Q167V3)	
SODIUM LAURYL SULFATE (UNII: 368GB5141J)	
TITANIUM DIOXIDE (UNII: 15FIX9V2JP)	

Product Characteristics

Color	PINK (Opaque pink body) , PINK (Opaque pink cap)	**Score**	no score
Shape	CAPSULE	**Size**	3mm
Flavor		**Imprint Code**	S6;10
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:43547-602-10	100 in 1 BOTTLE; Type 0: Not a Combination Product	09/01/2023	

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA216266	09/01/2023	

LISDEXAMFETAMINE DIMESYLATE

lisdexamfetamine dimesylate capsules capsule

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:43547-603
Route of Administration	ORAL	**DEA Schedule**	CII

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
LISDEXAMFETAMINE DIMESYLATE (UNII: SJT761GEGS) (LISDEXAMFETAMINE - UNII:H645GUL8KJ)	LISDEXAMFETAMINE DIMESYLATE	20 mg

Inactive Ingredients

Ingredient Name	Strength
CROSCARMELLOSE SODIUM (UNII: M28OL1HH48)	
D&C YELLOW NO. 10 ALUMINUM LAKE (UNII: CQ3XH3DET6)	
FD&C BLUE NO. 1--ALUMINUM LAKE (UNII: J9EQA3S2JM)	
FD&C BLUE NO. 2--ALUMINUM LAKE (UNII: 4AQJ3LG584)	
FD&C RED NO. 40 (UNII: WZB9127XOA)	
FERRIC OXIDE YELLOW (UNII: EX438O2MRT)	
FERROSOFERRIC OXIDE (UNII: XM0M87F357)	
GELATIN, UNSPECIFIED (UNII: 2G86QN327L)	
MAGNESIUM STEARATE (UNII: 70097M6I30)	
MICROCRYSTALLINE CELLULOSE (UNII: OP1R32D61U)	
POTASSIUM HYDROXIDE (UNII: WZH3C48M4T)	
PROPYLENE GLYCOL (UNII: 6DC9Q167V3)	

SODIUM LAURYL SULFATE (UNII: 368GB5141J)	
TITANIUM DIOXIDE (UNII: 15FIX9V2JP)	

Product Characteristics

Color	WHITE (Opaque ivory body) , WHITE (Opaque ivory cap)	**Score**	no score
Shape	CAPSULE	**Size**	3mm
Flavor		**Imprint Code**	S6;20
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:43547-603-10	100 in 1 BOTTLE; Type 0: Not a Combination Product	09/01/2023	

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA216266	09/01/2023	

LISDEXAMFETAMINE DIMESYLATE

lisdexamfetamine dimesylate capsules capsule

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:43547-604
Route of Administration	ORAL	**DEA Schedule**	CII

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
LISDEXAMFETAMINE DIMESYLATE (UNII: SJT761GEGS) (LISDEXAMFETAMINE - UNII:H645GUL8KJ)	LISDEXAMFETAMINE DIMESYLATE	30 mg

Inactive Ingredients

Ingredient Name	Strength
CROSCARMELLOSE SODIUM (UNII: M28OL1HH48)	
D&C YELLOW NO. 10 ALUMINUM LAKE (UNII: CQ3XH3DET6)	
FD&C BLUE NO. 1--ALUMINUM LAKE (UNII: J9EQA3S2JM)	
FD&C BLUE NO. 2--ALUMINUM LAKE (UNII: 4AQJ3LG584)	
FD&C RED NO. 3 (UNII: PN2ZH5LOQY)	
FD&C RED NO. 40 (UNII: WZB9127XOA)	
FD&C YELLOW NO. 6 (UNII: H77VEI93A8)	

FERROSOFERRIC OXIDE (UNII: XM0M87F357)	
GELATIN, UNSPECIFIED (UNII: 2G86QN327L)	
MAGNESIUM STEARATE (UNII: 70097M6I30)	
MICROCRYSTALLINE CELLULOSE (UNII: OP1R32D61U)	
POTASSIUM HYDROXIDE (UNII: WZH3C48M4T)	
PROPYLENE GLYCOL (UNII: 6DC9Q167V3)	
SODIUM LAURYL SULFATE (UNII: 368GB5141J)	
TITANIUM DIOXIDE (UNII: 15FIX9V2JP)	

Product Characteristics

Color	WHITE (Opaque white body) , ORANGE (Opaque orange cap)	**Score**	no score
Shape	CAPSULE	**Size**	3mm
Flavor		**Imprint Code**	S6;30
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:43547-604-10	100 in 1 BOTTLE; Type 0: Not a Combination Product	09/01/2023	

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA216266	09/01/2023	

LISDEXAMFETAMINE DIMESYLATE

lisdexamfetamine dimesylate capsules capsule

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:43547-605
Route of Administration	ORAL	**DEA Schedule**	CII

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
LISDEXAMFETAMINE DIMESYLATE (UNII: SJT761GEGS) (LISDEXAMFETAMINE - UNII:H645GUL8KJ)	LISDEXAMFETAMINE DIMESYLATE	40 mg

Inactive Ingredients

Ingredient Name	Strength
CROSCARMELLOSE SODIUM (UNII: M28OL1HH48)	
D&C YELLOW NO. 10 ALUMINUM LAKE (UNII: CQ3XH3DET6)	

FD&C BLUE NO. 1 (UNII: H3R47K3TBD)	
FD&C BLUE NO. 1--ALUMINUM LAKE (UNII: J9EQA3S2JM)	
FD&C BLUE NO. 2--ALUMINUM LAKE (UNII: 4AQJ3LG584)	
FD&C RED NO. 40 (UNII: WZB9127XOA)	
FERRIC OXIDE YELLOW (UNII: EX438O2MRT)	
FERROSOFERRIC OXIDE (UNII: XM0M87F357)	
GELATIN, UNSPECIFIED (UNII: 2G86QN327L)	
MAGNESIUM STEARATE (UNII: 70097M6I30)	
MICROCRYSTALLINE CELLULOSE (UNII: OP1R32D61U)	
POTASSIUM HYDROXIDE (UNII: WZH3C48M4T)	
PROPYLENE GLYCOL (UNII: 6DC9Q167V3)	
SODIUM LAURYL SULFATE (UNII: 368GB5141J)	
TITANIUM DIOXIDE (UNII: 15FIX9V2JP)	

Product Characteristics

Color	WHITE (Opaque white body) , BLUE (Opaque blue green cap)	**Score**	no score
Shape	CAPSULE	**Size**	3mm
Flavor		**Imprint Code**	S6;40
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:43547-605-10	100 in 1 BOTTLE; Type 0: Not a Combination Product	09/01/2023	

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA216266	09/01/2023	

LISDEXAMFETAMINE DIMESYLATE

lisdexamfetamine dimesylate capsules capsule

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:43547-606
Route of Administration	ORAL	**DEA Schedule**	CII

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
LISDEXAMFETAMINE DIMESYLATE (UNII: SJT761GEGS) (LISDEXAMFETAMINE - UNII:H645GUL8KJ)	LISDEXAMFETAMINE DIMESYLATE	50 mg

Inactive Ingredients

Ingredient Name	Strength
CROSCARMELLOSE SODIUM (UNII: M28OL1HH48)	
D&C YELLOW NO. 10 ALUMINUM LAKE (UNII: CQ3XH3DET6)	
FD&C BLUE NO. 1 (UNII: H3R47K3TBD)	
FD&C BLUE NO. 1--ALUMINUM LAKE (UNII: J9EQA3S2JM)	
FD&C BLUE NO. 2--ALUMINUM LAKE (UNII: 4AQJ3LG584)	
FD&C RED NO. 40 (UNII: WZB9127XOA)	
FERROSOFERRIC OXIDE (UNII: XM0M87F357)	
GELATIN, UNSPECIFIED (UNII: 2G86QN327L)	
MAGNESIUM STEARATE (UNII: 70097M6I30)	
MICROCRYSTALLINE CELLULOSE (UNII: OP1R32D61U)	
POTASSIUM HYDROXIDE (UNII: WZH3C48M4T)	
PROPYLENE GLYCOL (UNII: 6DC9Q167V3)	
SODIUM LAURYL SULFATE (UNII: 368GB5141J)	
TITANIUM DIOXIDE (UNII: 15FIX9V2JP)	

Product Characteristics

Color	WHITE (Opaque white body) , BLUE (Opaque bule cap)	**Score**	no score
Shape	CAPSULE	**Size**	3mm
Flavor		**Imprint Code**	S6;50
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:43547-606-10	100 in 1 BOTTLE; Type 0: Not a Combination Product	09/01/2023	

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA216266	09/01/2023	

LISDEXAMFETAMINE DIMESYLATE

lisdexamfetamine dimesylate capsules capsule

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:43547-607
Route of Administration	ORAL	**DEA Schedule**	CII

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
LISDEXAMFETAMINE DIMESYLATE (UNII: SJT761GEGS) (LISDEXAMFETAMINE - UNII:H645GUL8KJ)	LISDEXAMFETAMINE DIMESYLATE	60 mg

Inactive Ingredients

Ingredient Name	Strength
CROSCARMELLOSE SODIUM (UNII: M28OL1HH48)	
D&C YELLOW NO. 10 ALUMINUM LAKE (UNII: CQ3XH3DET6)	
FD&C BLUE NO. 1 (UNII: H3R47K3TBD)	
FD&C BLUE NO. 1--ALUMINUM LAKE (UNII: J9EQA3S2JM)	
FD&C BLUE NO. 2--ALUMINUM LAKE (UNII: 4AQJ3LG584)	
FD&C RED NO. 40 (UNII: WZB9127XOA)	
FERROSOFERRIC OXIDE (UNII: XM0M87F357)	
GELATIN, UNSPECIFIED (UNII: 2G86QN327L)	
MAGNESIUM STEARATE (UNII: 70097M6I30)	
MICROCRYSTALLINE CELLULOSE (UNII: OP1R32D61U)	
POTASSIUM HYDROXIDE (UNII: WZH3C48M4T)	
PROPYLENE GLYCOL (UNII: 6DC9Q167V3)	
SODIUM LAURYL SULFATE (UNII: 368GB5141J)	
TITANIUM DIOXIDE (UNII: 15FIX9V2JP)	

Product Characteristics

Color	BLUE (Opaque aqua blue body) , BLUE (Opaque aqua blue cap)	**Score**	no score
Shape	CAPSULE	**Size**	3mm
Flavor		**Imprint Code**	S6;60
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:43547-607-10	100 in 1 BOTTLE; Type 0: Not a Combination Product	09/01/2023	

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA216266	09/01/2023	

LISDEXAMFETAMINE DIMESYLATE

lisdexamfetamine dimesylate capsules capsule

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	Item Code (Source)	NDC:43547-608
Route of Administration	ORAL	DEA Schedule	CII

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
LISDEXAMFETAMINE DIMESYLATE (UNII: SJT761GEGS) (LISDEXAMFETAMINE - UNII:H645GUL8KJ)	LISDEXAMFETAMINE DIMESYLATE	70 mg

Inactive Ingredients

Ingredient Name	Strength
CROSCARMELLOSE SODIUM (UNII: M28OL1HH48)	
D&C YELLOW NO. 10 ALUMINUM LAKE (UNII: CQ3XH3DET6)	
FD&C BLUE NO. 1 (UNII: H3R47K3TBD)	
FD&C BLUE NO. 1--ALUMINUM LAKE (UNII: J9EQA3S2JM)	
FD&C BLUE NO. 2--ALUMINUM LAKE (UNII: 4AQJ3LG584)	
FD&C RED NO. 3 (UNII: PN2ZH5LOQY)	
FD&C RED NO. 40 (UNII: WZB9127XOA)	
FD&C YELLOW NO. 6 (UNII: H77VEI93A8)	
FERROSOFERRIC OXIDE (UNII: XM0M87F357)	
GELATIN, UNSPECIFIED (UNII: 2G86QN327L)	
MAGNESIUM STEARATE (UNII: 70097M6I30)	
MICROCRYSTALLINE CELLULOSE (UNII: OP1R32D61U)	
POTASSIUM HYDROXIDE (UNII: WZH3C48M4T)	
PROPYLENE GLYCOL (UNII: 6DC9Q167V3)	
SODIUM LAURYL SULFATE (UNII: 368GB5141J)	
TITANIUM DIOXIDE (UNII: 15FIX9V2JP)	

Product Characteristics

Color	BLUE (Opaque blue body) , ORANGE (Opaque orange cap)	**Score**	no score
Shape	CAPSULE	**Size**	3mm
Flavor		**Imprint Code**	S6;70
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:43547-608-10	100 in 1 BOTTLE; Type 0: Not a Combination Product	09/01/2023	

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA216266	09/01/2023	

Labeler - Solco Healthcare US,LLC (828343017)

Registrant - Prinston Pharmaceutical Inc (967289799)

Establishment

Name	Address	ID/FEI	Business Operations
Generics Bidco II LLC		151228897	MANUFACTURE(43547-602, 43547-603, 43547-604, 43547-605, 43547-606, 43547-607, 43547-608)

Revised: 3/2023 Solco Healthcare US,LLC