DEXEDRINE SPANSULE- dextroamphetamine sulfate capsule, extended release
Amneal Pharmaceuticals LLC

DEXEDRINE®
(dextroamphetamine sulfate) SPANSULE® sustained-release capsules, CII
Rx Only

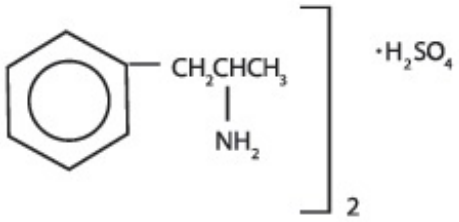
WARNING: ABUSE, MISUSE, AND ADDICTION

DEXEDRINE has a high potential for abuse and misuse, which can lead to the development of a substance use disorder, including addiction. Misuse and abuse of CNS stimulants, including DEXEDRINE, can result in overdose and death *[see Overdosage]*, and this risk is increased with higher doses or unapproved methods of administration, such as snorting or injection.
Before prescribing DEXEDRINE, assess each patient's risk for abuse, misuse, and addiction. Educate patients and their families about these risks, proper storage of the drug, and proper disposal of any unused drug. Throughout DEXEDRINE treatment, reassess each patient's risk of abuse, misuse, and addiction and frequently monitor for signs and symptoms of abuse, misuse, and addiction *[see Warnings* and *Drug Abuse and Dependence]*.

DESCRIPTION

DEXEDRINE (dextroamphetamine sulfate) is the dextro isomer of the compound *d*,*l*-amphetamine sulfate, a sympathomimetic amine of the amphetamine group. Chemically, dextroamphetamine is *d*-alpha-methylphenethylamine, and is present in all forms of DEXEDRINE as the neutral sulfate.

Structural formula:



SPANSULE capsules

Each SPANSULE sustained-release capsule is so prepared that an initial dose is released promptly and the remaining medication is released gradually over a prolonged period.

Each capsule, with brown cap and natural body, contains dextroamphetamine sulfate. The 5-mg capsule is imprinted in white with IX and 5 mg on the brown cap and is imprinted in white with 673 and 5 mg on the natural body. The 10-mg capsule is

imprinted in white with IX and 10 mg on the brown cap and is imprinted in white with 674 and 10 mg on the natural body. The 15-mg capsule is imprinted in white with IX and 15 mg on the brown cap and is imprinted in white with 675 and 15 mg on the natural body. Product reformulation in 1996 has caused a minor change in the color of the time-released pellets within each capsule. Inactive ingredients now consist of cetyl alcohol, D&C Yellow No. 10, dibutyl sebacate, ethylcellulose, FD&C Blue No. 1, FD&C Red No. 40, FD&C Yellow No. 6, gelatin, hypromellose, polyethylene glycol, povidone, sodium lauryl sulfate, sugar spheres, and trace amounts of other inactive ingredients.

CLINICAL PHARMACOLOGY

Amphetamines are noncatecholamine, sympathomimetic amines with CNS stimulant activity. Peripheral actions include elevations of systolic and diastolic blood pressures and weak bronchodilator and respiratory stimulant action. There is neither specific evidence that clearly establishes the mechanism whereby amphetamines produce mental and behavioral effects in children, nor conclusive evidence regarding how these effects relate to the condition of the central nervous system. DEXEDRINE SPANSULE Capsules are formulated to release the active drug substance *in vivo* in a more gradual fashion than the standard formulation, as demonstrated by blood levels. The formulation has not been shown superior in effectiveness over the same dosage of the standard, noncontrolled-release formulations given in divided doses.

Pharmacokinetics

The pharmacokinetics of the tablet and sustained-release capsule were compared in 12 healthy subjects. The extent of bioavailability of the sustained-release capsule was similar compared to the immediate-release tablet. Following administration of three 5-mg tablets, average maximal dextroamphetamine plasma concentrations (C_{max}) of 36.6 ng/mL were achieved at approximately 3 hours.

Following administration of one 15-mg sustained-release capsule, maximal dextroamphetamine plasma concentrations were obtained approximately 8 hours after dosing. The average C_{max} was 23.5 ng/mL. The average plasma $T_{½}$ was similar for both the tablet and sustained-release capsule and was approximately 12 hours. In 12 healthy subjects, the rate and extent of dextroamphetamine absorption were similar following administration of the sustained-release capsule formulation in the fed (58 g to 75 g fat) and fasted state.

INDICATIONS AND USAGE

DEXEDRINE is indicated in:

Narcolepsy

Attention Deficit Disorder with Hyperactivity

As an integral part of a total treatment program that typically includes other measures (psychological, educational, social) for patients (ages 6 years to 16 years) with this syndrome. A diagnosis of Attention Deficit Hyperactivity Disorder (ADHD; DSM-IV) implies the presence of the hyperactive-impulsive or inattentive symptoms that caused impairment and were present before age 7 years. The symptoms must cause clinically significant impairment, e.g., in social, academic, or occupational functioning, and be

present in 2 or more settings, e.g., school (or work) and at home. The symptoms must not be better accounted for by another mental disorder. For the Inattentive Type, at least 6 of the following symptoms must have persisted for at least 6 months: lack of attention to details/careless mistakes; lack of sustained attention; poor listener; failure to follow through on tasks; poor organization; avoids tasks requiring sustained mental effort; loses things; easily distracted; forgetful. For the Hyperactive-Impulsive Type, at least 6 of the following symptoms must have persisted for at least 6 months: fidgeting/squirming; leaving seat; inappropriate running/climbing; difficulty with quiet activities; “on the go”; excessive talking; blurting answers; can't wait turn; intrusive. The Combined Type requires both inattentive and hyperactive-impulsive criteria to be met.

Special Diagnostic Considerations

Specific etiology of this syndrome is unknown, and there is no single diagnostic test. Adequate diagnosis requires the use of medical and special psychological, educational, and social resources. Learning may or may not be impaired. The diagnosis must be based upon a complete history and evaluation of the patient and not solely on the presences of the required number of DSM-IV characteristics.

Need for Comprehensive Treatment Program

DEXEDRINE is indicated as an integral part of a total treatment program for ADHD that may include other measures (psychological, educational, social) for patients with this syndrome. Drug treatment may not be indicated for all patients with this syndrome. Stimulants are not intended for use in patients who exhibit symptoms secondary to environmental factors and/or other primary psychiatric disorders, including psychosis. Appropriate educational placement is essential and psychosocial intervention is often helpful. When remedial measures alone are insufficient, the decision to prescribe stimulant medication will depend upon the physician’s assessment of the chronicity and severity of the patient’s symptoms.

CONTRAINDICATIONS

In patients known to be hypersensitive to amphetamine, or other components of DEXEDRINE. Hypersensitivity reactions such as angioedema and anaphylactic reactions have been reported in patients treated with other amphetamine products *[see Adverse Reactions]*.

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 *Drug Interactions]*.

WARNINGS

Abuse, Misuse, and Addiction

DEXEDRINE has a high potential for abuse and misuse. The use of DEXEDRINE exposes individuals to the risks of abuse and misuse, which can lead to the development of a substance use disorder, including addiction. DEXEDRINE can be diverted for non-medical use into illicit channels or distribution *[see Drug Abuse and Dependence]*. Misuse and abuse of CNS stimulants, including DEXEDRINE can result in overdose and death *[see Overdosage]*, and this risk is increased with higher doses or unapproved methods

of administration, such as snorting or injection.

Before prescribing DEXEDRINE, assess each patient's risk for abuse, misuse, and addiction. Educate patients and their families about these risks and proper disposal of any unused drug. Advise patients to store amphetamine sulfate in a safe place, preferably locked, and instruct patients to not give DEXEDRINE to anyone else. Throughout DEXEDRINE treatment, reassess each patient's risk of abuse, misuse, and addiction and frequently monitor for signs and symptoms of abuse, misuse, and addiction.

Risks to Patients with Serious Cardiac Disease

Sudden death has been reported in patients with structural cardiac abnormalities or other serious cardiac disease who are treated with CNS stimulants at the recommended ADHD dosages.

Avoid DEXEDRINE use in patients with known structural cardiac abnormalities, cardiomyopathy, serious cardiac arrhythmia, coronary artery disease, or other serious cardiac disease.

Increased Blood Pressure and Heart Rate

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.

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 Disease

CNS stimulants may induce a manic or mixed episode in patients. 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, or 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. In a pooled analysis of multiple short-term, placebo-controlled studies of CNS stimulants, psychotic or manic symptoms occurred in approximately 0.1% of CNS stimulant-treated patients, compared with 0% of placebo-treated patients. If such symptoms occur, consideration discontinuing DEXEDRINE.

Long-Term Suppression of Growth in Pediatric Patients

CNS stimulants have been associated with weight loss and slowing of growth rate in pediatric patients, including DEXEDRINE. Closely monitor growth (weight and height) in DEXEDRINE -treated pediatric patients treated with CNS stimulants.

Pediatric patients who are not growing or gaining height or weight as expected may need to have their treatment interrupted *[see **Precautions, Pediatric Use**]*.

Seizures

There is some clinical evidence that stimulants may lower the convulsive threshold in patients with prior history of seizures, in patients with prior EEG abnormalities in absence of seizures, and, very rarely, in patients without a history of seizures and no prior EEG evidence of seizures. In the presence of seizures, the drug should be discontinued.

Peripheral Vasculopathy, including Raynaud's phenomenon

Stimulants, including DEXEDRINE, used to treat ADHD are associated with peripheral vasculopathy, including Raynaud's phenomenon. Signs and symptoms are usually intermittent and mild; however, sequelae have included digital ulceration and/or soft tissue breakdown. Effects of peripheral vasculopathy, including Raynaud's phenomenon, were observed in post-marketing reports and at therapeutic dosages in all age groups throughout the course of treatment. Signs and symptoms generally improve after dosage reduction or discontinuation of the CNS stimulant. Careful observation for digital changes is necessary during DEXEDRINE treatment. Further clinical evaluation (e.g., rheumatology referral) may be appropriate for DEXEDRINE-treated patients who develop signs or symptoms of peripheral vasculopathy.

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]*. Amphetamines and amphetamine derivatives are known to be metabolized, to some degree, by cytochrome P450 2D6 (CYP2D6) and display minor inhibition of CYP2D6 metabolism *[see Clinical Pharmacology]*. The potential for a pharmacokinetic interaction exists with the co-administration of CYP2D6 inhibitors which may increase the risk with increased exposure to DEXEDRINE. In these situations, consider an alternative non-serotonergic drug or an alternative drug that does not inhibit CYP2D6 *[see Drug Interactions]*.

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 DEXEDRINE with MAOI drugs is contraindicated *[see Contraindications]*.

Discontinue treatment with DEXEDRINE and any concomitant serotonergic agents immediately if the above symptoms occur, and initiate supportive symptomatic treatment. If concomitant use of DEXEDRINE with other serotonergic drugs or CYP2D6 inhibitors is clinically warranted, initiate DEXEDRINE 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.

Motor and Verbal Tics, and Worsening of Tourette's Syndrome

CNS stimulants, including amphetamine sulfate, have been associated with the onset or

exacerbation of motor and verbal tics. Worsening of Tourette's syndrome has also been reported. Before initiating DEXEDRINE, assess the family history and clinically evaluate patients for tics or Tourette's syndrome. Regularly monitor patients for the emergence or worsening of tics or Tourette's syndrome with DEXEDRINE, and discontinue treatment if clinically appropriate.

PRECAUTIONS

General

The least amount feasible should be prescribed or dispensed at 1 time in order to minimize the possibility of overdosage.

Information for Patients

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

Abuse, Misuse, and Addiction

Educate patients and their families about the risks of abuse, misuse, and addiction of DEXEDRINE, which can lead to overdose and death, and proper disposal of any unused drug *[see Warnings, Drug Abuse and Dependence, Overdosage]*. Advise patients to store DEXEDRINE in a safe place, preferably locked, and instruct patients to not give DEXEDRINE to anyone else.

Risks to Patients with Serious Cardiac Disease

Advise patients that there are potential risks to patients with serious cardiac disease, including sudden death, with DEXEDRINE 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]*.

Increased Blood Pressure and Heart Rate

Instruct patients that DEXEDRINE can elevate blood pressure and heart rate *[see Warnings]*.

Psychiatric Adverse Reactions

Advise patients that DEXEDRINE, at recommended doses, can cause psychotic or manic symptoms, even in patients without prior history of psychotic symptoms or mania *[see Warnings]*.

Long-Term Suppression of Growth in Pediatric Patients

Advise patients that DEXEDRINE may cause slowing of growth and weight loss in pediatric patients *[see Warnings]*.

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

- Instruct patients beginning treatment with DEXEDRINE 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 color 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 DEXEDRINE.**
- Further clinical evaluation (e.g., rheumatology referral) may be appropriate for certain patients *[see Warnings]*.

Motor and Verbal Tics, and Worsening of Tourette's Syndrome

Advise patients that motor and verbal tics and worsening of Tourette's Syndrome may occur during treatment with DEXEDRINE. Instruct the patients to notify their healthcare provider if emergence or worsening of tics or Tourette's syndrome occurs *[see Warnings]*.

Drug Interactions

Acidifying Agents

Lower blood levels and efficacy of amphetamines. Increase dose based on clinical response. Examples of acidifying agents include gastrointestinal acidifying agents (e.g., guanethidine, reserpine, glutamic acid HCl, ascorbic acid) and urinary acidifying agents (e.g., ammonium chloride, sodium acid phosphate, methenamine salts).

Adrenergic Blockers

Adrenergic blockers are inhibited by amphetamines.

Alkalinizing Agents

Increase blood levels and potentiate the action of amphetamine. Co-administration of DEXEDRINE and gastrointestinal alkalinizing agents should be avoided. Examples of alkalinizing agents include gastrointestinal alkalinizing agents (e.g., sodium bicarbonate) and urinary alkalinizing agents (e.g. acetazolamide, some thiazides).

Tricyclic Antidepressants

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. Monitor frequently and adjust or use alternative therapy based on clinical response. Examples of tricyclic antidepressants include desipramine, Protriptyline.

CYP2D6 Inhibitors

The concomitant use of DEXEDRINE and CYP2D6 inhibitors may increase the exposure of DEXEDRINE compared to the use of the drug alone and increase the risk of serotonin syndrome. Initiate with lower doses and monitor patients for signs and symptoms of serotonin syndrome particularly during DEXEDRINE initiation and after a dosage increase. If serotonin syndrome occurs, discontinue DEXEDRINE and the CYP2D6 inhibitor *[see Warnings, Overdosage]*. Examples of CYP2D6 Inhibitors include paroxetine and fluoxetine (also serotonergic drugs), quinidine, ritonavir.

Serotonergic Drugs

The concomitant use of DEXEDRINE and serotonergic drugs increases the risk of serotonin syndrome. Initiate with lower doses and monitor patients for signs and symptoms of serotonin syndrome, particularly during DEXEDRINE initiation or dosage increase. If serotonin syndrome occurs, discontinue DEXEDRINE and the concomitant

serotonergic drug(s) *[see Warnings and Precautions]*. Examples of serotonergic drugs include selective serotonin reuptake inhibitors (SSRI), serotonin norepinephrine reuptake inhibitors (SNRI), triptans, tricyclic antidepressants, fentanyl, lithium, tramadol, tryptophan, buspirone, St. John's Wort.

MAO Inhibitors

Concomitant use of MAOIs and CNS stimulants can cause hypertensive crisis. Potential outcomes include death, stroke, myocardial infarction, aortic dissection, ophthalmological complications, eclampsia, pulmonary edema, and renal failure. Do not administer DEXEDRINE concomitantly or within 14 days after discontinuing MAOI *[see Contraindications* and *Warnings]*. Examples of MAOIs include selegiline, tranylcypromine, isocarboxazid, phenelzine, linezolid, methylene blue.

Proton Pump Inhibitors

Time to maximum concentration (T_{max}) of amphetamine is decreased compared to when administered alone. Monitor patients for changes in clinical effect and adjust therapy based on clinical response. An example of a proton pump inhibitor is omeprazole.

Antihistamines

Amphetamines may counteract the sedative effect of antihistamines.

Antihypertensives

Amphetamines may antagonize the hypotensive effects of antihypertensives.

Chlorpromazine

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

Ethosuximide

Amphetamines may delay intestinal absorption of ethosuximide.

Haloperidol

Haloperidol blocks dopamine and norepinephrine reuptake, thus inhibiting the central stimulant effects of amphetamines.

Lithium Carbonate

The stimulatory effects of amphetamines may be inhibited by lithium carbonate.

Meperidine

Amphetamines potentiate the analgesic effect of meperidine.

Methenamine Therapy

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

Norepinephrine

Amphetamines enhance the adrenergic effect of norepinephrine.

Phenobarbital

Amphetamines may delay intestinal absorption of phenobarbital; co-administration of phenobarbital may produce a synergistic anticonvulsant action.

Phenytoin

Amphetamines may delay intestinal absorption of phenytoin; co-administration of phenytoin may produce a synergistic anticonvulsant action.

Propoxyphene

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

Veratrum Alkaloids

Amphetamines inhibit the hypotensive effect of veratrum alkaloids.

Drug/Laboratory Test Interactions

Amphetamines can cause a significant elevation in plasma corticosteroid levels. This increase is greatest in the evening.

Amphetamines may interfere with urinary steroid determinations.

Carcinogenesis/Mutagenesis

Mutagenicity studies and long-term studies in animals to determine the carcinogenic potential of DEXEDRINE have not been performed.

Pregnancy

Teratogenic Effects

DEXEDRINE has been shown to have embryotoxic and teratogenic effects when administered to A/Jax mice and C57BL mice in doses approximately 41 times the maximum human dose. Embryotoxic effects were not seen in New Zealand white rabbits given the drug in doses 7 times the human dose nor in rats given 12.5 times the maximum human dose. While there are no adequate and well-controlled studies in pregnant women, there has been 1 report of severe congenital bony deformity, tracheoesophageal fistula, and anal atresia (VATER association) in a baby born to a woman who took dextroamphetamine sulfate with lovastatin during the first trimester of pregnancy. DEXEDRINE should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nonteratogenic Effects

Infants born to mothers dependent on amphetamines have an increased risk of premature delivery and low birth weight. Also, these infants may experience symptoms of withdrawal as demonstrated by dysphoria, including agitation, and significant lassitude.

Nursing Mothers

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

Pediatric Use

Long-term effects of amphetamines in pediatric patients have not been well established.

DEXEDRINE is not recommended for use in pediatric patients younger than 6 years of age with Attention Deficit Disorder with Hyperactivity described under INDICATIONS AND USAGE.

Clinical experience suggests that in psychotic children, administration of amphetamines may exacerbate symptoms of behavior disturbance and thought disorder.

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

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

Drug treatment is not indicated in all cases of Attention Deficit Disorder with Hyperactivity and should be considered only in light of the complete history and evaluation of the child. The decision to prescribe amphetamines should depend on the physician's assessment of the chronicity and severity of the child's symptoms and their appropriateness for his or her age. Prescription should not depend solely on the presence of one or more of the behavioral characteristics.

When these symptoms are associated with acute stress reactions, treatment with amphetamines is usually not indicated.

ADVERSE REACTIONS

Cardiovascular

Palpitations, tachycardia, elevation of blood pressure. There have been isolated reports of cardiomyopathy associated with chronic amphetamine use.

Central Nervous System

Psychotic episodes at recommended doses (rare), overstimulation, restlessness, dizziness, insomnia, euphoria, dyskinesia, dysphoria, tremor, headache, exacerbation of motor and verbal tics, and Tourette's syndrome.

Gastrointestinal

Dryness of the mouth, unpleasant taste, diarrhea, constipation, intestinal ischemia, and other gastrointestinal disturbances. Anorexia and weight loss may occur as undesirable effects.

Allergic

Urticaria.

Endocrine

Impotence, changes in libido, frequent or prolonged erections.

Musculoskeletal

Rhabdomyolysis.

Skin and Subcutaneous Tissue Disorders

Alopecia.

To report SUSPECTED ADVERSE REACTIONS, contact Amneal Pharmaceuticals at 1-877-835-5472 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

DRUG ABUSE AND DEPENDENCE

Controlled Substance

DEXEDRINE contains dextroamphetamine, a Schedule II controlled substance.

Abuse

DEXEDRINE has a high potential for abuse and misuse which can lead to the development of a substance use disorder, including addiction *[see Warnings]*. DEXEDRINE can be diverted for non-medical use into illicit channels or distribution.

Abuse is the intentional non-therapeutic use of a drug, even once, to achieve a desired psychological or physiological effect. Misuse is the intentional use, for therapeutic purposes, of a drug by an individual in a way other than prescribed by a health care provider or for whom it was not prescribed. 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 a higher priority to drug use than other activities and obligations), and possible tolerance or physical dependence.

Misuse and abuse of amphetamine may cause increased heart rate, respiratory rate, or blood pressure; sweating; dilated pupils; hyperactivity; restlessness; insomnia; decreased appetite; loss of coordination; tremors; flushed skin; vomiting; and/or abdominal pain. Anxiety, psychosis, hostility, aggression, and suicidal or homicidal ideation have also been observed with CNS stimulants abuse and/or misuse. Misuse and abuse of CNS stimulants, including DEXEDRINE, can result in overdose and death *[see Overdosage]*, and this risk is increased with higher doses or unapproved methods of administration, such as snorting or injection.

Dependence

Physical Dependence

DEXEDRINE may produce physical dependence. Physical dependence is a state that develops as a result of physiological adaptation in response to repeated drug use, manifested by withdrawal signs and symptoms after abrupt discontinuation or a significant dose reduction of a drug.

Withdrawal signs and symptoms after abrupt discontinuation or dose reduction following prolonged use of CNS stimulants including DEXEDRINE include dysphoric mood; depression; fatigue; vivid, unpleasant dreams; insomnia or hypersomnia; increased appetite; and psychomotor retardation or agitation.

Tolerance

DEXEDRINE may produce tolerance. Tolerance is a physiological state characterized by a reduced response to a drug after repeated administration (i.e., a higher dose of a drug is required to produce the same effect that was once obtained at a lower dose).

OVERDOSAGE

Clinical Effects of Overdose

Overdose of CNS stimulants is characterized by the following sympathomimetic effects:

- Cardiovascular effects including tachyarrhythmias, and hypertension or hypotension. Vasospasm, myocardial infarction, or aortic dissection may precipitate sudden cardiac death. Takotsubo cardiomyopathy may develop.
- CNS effects including psychomotor agitation, confusion, and hallucinations. Serotonin syndrome, seizures, cerebral vascular accidents, and coma may occur.
- Life-threatening hyperthermia (temperatures greater than 104°F) and rhabdomyolysis may develop.

Overdose Management

Consider the possibility of multiple drug ingestion. The prolonged release of amphetamine from DEXEDRINE should be considered when treating patients with overdose. D-amphetamine is not dialyzable. Consider contacting the Poison Help line (1-800-222-1222) or a medical toxicologist for additional overdose management recommendations.

DOSAGE AND ADMINISTRATION

Amphetamines should be administered at the lowest effective dosage and dosage should be individually adjusted. Late evening doses should be avoided because of the resulting insomnia.

Prior to treating patients with DEXEDRINE assess:

- for the presence of cardiac disease (i.e., perform a careful history, family history of sudden death or ventricular arrhythmia, and physical exam) *[see Warnings]*.
- the family history and clinically evaluate patients for motor or verbal tics or Tourette's syndrome *[see Warnings]*.

Narcolepsy

Usual dose is 5 to 60 mg per day in divided doses, depending on the individual patient response.

Narcolepsy seldom occurs in children under 12 years of age; however, when it does, DEXEDRINE may be used. The suggested initial dose for patients aged 6 to 12 is 5 mg daily; daily dose may be raised in increments of 5 mg at weekly intervals until an optimal response is obtained. In patients 12 years of age and older, start with 10 mg daily; daily dosage may be raised in increments of 10 mg at weekly intervals until an optimal response is obtained. If bothersome adverse reactions appear (e.g., insomnia or anorexia), dosage should be reduced.

SPANSULE capsules may be used for once-a-day dosage wherever appropriate.

Attention Deficit Disorder with Hyperactivity

The SPANSULE capsule formulation is not recommended for pediatric patients younger than 6 years of age.

In pediatric patients 6 years of age and older, start with 5 mg once or twice daily; daily dosage may be raised in increments of 5 mg at weekly intervals until optimal response is obtained. Only in rare cases will it be necessary to exceed a total of 40 mg per day. SPANSULE capsules may be used for once-a-day dosage wherever appropriate.

HOW SUPPLIED

DEXEDRINE SPANSULE capsules

Each capsule, with brown cap and natural body, contains dextroamphetamine sulfate.

The 5-mg capsule is imprinted in white with IX and 5 mg on the brown cap and is imprinted in white with 673 and 5 mg on the natural body.

The 10-mg capsule is imprinted in white with IX and 10 mg on the brown cap and is imprinted in white with 674 and 10 mg on the natural body.

The 15-mg capsule is imprinted in white with IX and 15 mg on the brown cap and is imprinted in white with 675 and 15 mg on the natural body.

5 mg 90s:	NDC 64896-673-10
10 mg 90s:	NDC 64896-674-10
15 mg 90s:	NDC 64896-675-10

Store at controlled room temperature between 20° to 25°C (68° to 77°F) [see USP].

Dispense in a tight, light-resistant container.

Manufactured by:
Catalent Pharma Solutions
Winchester, KY 40391

Distributed by:
Amneal Specialty, a division of
Amneal Pharmaceuticals LLC
Bridgewater, NJ 08807

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For additional copies of the printed medication guide, please visit www.amneal.com or contact us at 1-877-835-5472.

MEDICATION GUIDE

MEDICATION GUIDE **DEXEDRINE®(dek-suh-drin)** **(dextroamphetamine sulfate) SPANSULE® sustained-release capsules, CII**
What is the most important information I should know about DEXEDRINE?

DEXEDRINE may cause serious side effects, including:

- **Abuse misuse, and addiction.** DEXEDRINE has a high chance for abuse and misuse and may lead to substance use problems, including addiction. Misuse and abuse of DEXEDRINE, other amphetamine containing medicines, and methylphenidate containing medicines, can lead to overdose and death. The risk of overdose and death is increased with higher doses of DEXEDRINE or when it is used in ways that are not approved, such as snorting or injection.
  - Your healthcare provider should check you or your child's risk for abuse, misuse, and addiction before starting treatment with DEXEDRINE and will monitor you or your child during treatment.
  - DEXEDRINE may lead to physical dependence after prolonged use, even if taken as directed by your healthcare provider.
  - Do not give DEXEDRINE to anyone else. See **"What is DEXEDRINE?"** for more information.
  - Keep DEXEDRINE in a safe place and properly dispose of any unused medicine. See **"How should I store DEXEDRINE?"** for more information.
  - Tell your healthcare provider if you or your child have ever abused or been dependent on alcohol, prescription medicines, or street drugs.

- **Risks for people with serious heart disease:** Sudden death has happened in people who have heart defects or other serious heart disease.
  Your healthcare provider should check you or your child carefully for heart problems before starting DEXEDRINE. Tell your healthcare provider if you or your child have any heart problems, heart disease, or heart defects.
  Call your healthcare provider right away 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 DEXEDRINE.
- **Increased blood pressure and heart rate.**
  Your healthcare provider should check you or your child's blood pressure and heart rate regularly during treatment with DEXEDRINE.
- **Mental (psychiatric) problems, including:**

  - new or worse behavior or 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 DEXEDRINE, especially hearing voices, seeing or believing things that are not real, or new manic symptoms.

What is DEXEDRINE?

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

- a sleep disorder called narcolepsy.
- Attention-Deficit Hyperactivity Disorder (ADHD) in children 6 to 17 years of age.

- DEXEDRINE may help increase attention and decrease impulsiveness and hyperactivity in people with ADHD.

It is not known if DEXEDRINE is safe and effective in children under 6 years of age.
DEXEDRINE is a federally controlled substance (CII) because it contains dextroamphetamine that can be a target for people who abuse prescription medicines or street drugs. Keep DEXEDRINE in a safe place to protect it from theft. Never give your DEXEDRINE to anyone else because it may cause death or harm them. Selling or giving away DEXEDRINE may harm others and is against the law.

Do not take DEXEDRINE if you or your child:

- are allergic to amphetamine products or any of the ingredients in DEXEDRINE. See the end of this Medication Guide for a complete list of ingredients in DEXEDRINE.
- are taking or have taken within the past 14 days, a medicine used to treat depression called a monoamine oxidase inhibitor (MAOI), including the antibiotic linezolid or the intravenous medicine methylene blue.

Before taking DEXEDRINE, tell your healthcare provider about all of your or your child's medical conditions, including if you or your child:

- have heart problems, heart disease, 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 seizures or have had an abnormal brain wave test (EEG)
- have circulation problems in fingers and toes
- have or had repeated movements or sounds (tics) or Tourette's syndrome, or have a family history of tics or Tourette's syndrome
- are pregnant or plan to become pregnant. It is not known if DEXEDRINE will harm the unborn baby. Tell your healthcare provider if you or your child become pregnant during treatment with DEXEDRINE.
- are breastfeeding or plan to breastfeed. DEXEDRINE passes into breast milk. You or your child should not breastfeed during treatment with DEXEDRINE. Talk to your healthcare provider about the est way to feed the baby during treatment with DEXEDRINE.

Tell your healthcare provider about all of the medicines that you or your child take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.
DEXEDRINE and some medicines may interact with each other and cause serious side effects. Sometimes the doses of other medicines will need to be changed during treatment with DEXEDRINE. Your healthcare provider will decide if DEXEDRINE can be taken with other medicines.
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

Know the medicines that you or your child take. Keep a list of your or your child's medicines with you to show your healthcare provider and pharmacist when you or your child get a new medicine.

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

How should DEXEDRINE be taken?

- Take DEXEDRINE exactly as prescribed by your or your child's healthcare provider.
- Your healthcare provider may change the dose if needed.
- DEXEDRINE DEXEDRINE is an extended-release capsule. It releases medicine into your body throughout the day.

If you or your child take too much DEXEDRINE, call your healthcare provider or Poison Help line at 1-800-222-1222 or go to the nearest hospital emergency room right away.

What are possible side effects of DEXEDRINE?

DEXEDRINE may cause serious side effects, including:

- See **"What is the most important information I should know about DEXEDRINE?"**
- **Slowing of growth (height and weight) in children.** Children should have their height and weight checked often during treatment with DEXEDRINE. Your healthcare provider may stop your child's DEXEDRINE treatment if they are not growing or gaining weight as expected.
- **Seizures**. Your healthcare provider may stop treatment with DEXEDRINE if you or your child have a seizure.
- **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 DEXEDRINE.

- **New or worsening tics or worsening Tourette's syndrome.** Tell your healthcare provider if you or your child get any new or worsening tics or worsening Tourette's syndrome during treatment with DEXEDRINE.
- **Serotonin syndrome.** This problem may happen when DEXEDRINE is taken with certain other medicines and may be life-threatening. Stop taking DEXEDRINE 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,
  - fast heartbeat
  - flushing
  - seizures
  - coma

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

The most common side effects of DEXEDRINE include:

- fast heartbeat
- decreased appetite
- tremors
- headache
- trouble sleeping
- dizziness
- stomach upset
- weight loss
- dry mouth

These are not all of the possible side effects of DEXEDRINE. 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 DEXEDRINE?

- Store DEXEDRINE at room temperature between 68° to 77°F (20° to 25°C).
- Store DEXEDRINE in a safe place, like a locked cabinet. Protect from light.
- Dispose of remaining, unused, or expired DEXEDRINE by a medicine take-back program at a U.S. Drug Enforcement Administration (DEA) authorized collection site. If no take-back program or DEA authorized collector is available, mix DEXEDRINE 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 DEXEDRINE in the household trash. Visit www.fda.gov/drugdisposal for additional information on disposal of unused medicines.

Keep DEXEDRINE and all medicines out of the reach of children.

General information about the safe and effective use of DEXEDRINE.

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. Do not use DEXEDRINE for a condition for which it was not prescribed. Do not give DEXEDRINE to other people, even if they have the same symptoms that you or your child have. It may harm them and it is against the law. You can ask your pharmacist or healthcare provider for information about DEXEDRINE that is written for healthcare professionals.

What are the ingredients in DEXEDRINE?

Active ingredient: dextroamphetamine sulfate

Inactive ingredients: cetyl alcohol, D&C Yellow No. 10, dibutyl sebacate, ethylcellulose, FD&C Blue No. 1, FD&C Red No. 40, FD&C Yellow No. 6, gelatin, hypromellose, polyethylene glycol, povidone, sodium lauryl sulfate, sugar spheres, and trace amounts of other inactive ingredients.

Manufactured by:
Catalent Pharma Solutions
Winchester, KY 40391
Distributed by:
Amneal Specialty, a division of
Amneal Pharmaceuticals LLC
Bridgewater, NJ 08807
For more information about DEXEDRINE, visit www.amneal.com or call 1-877-835-5472.

This Medication Guide has been approved by the U.S. Food and Drug Administration.
Rev. 10-2023-01

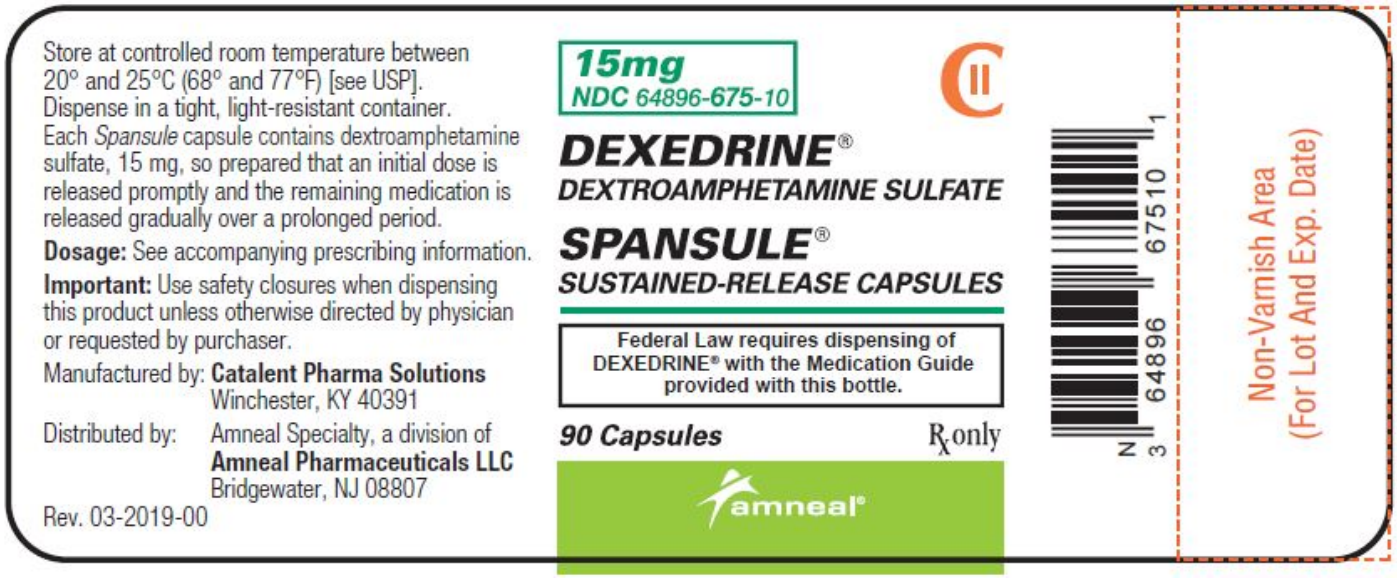
PRINCIPAL DISPLAY PANEL - 5 mg BOTTLE LABEL

PRINCIPAL DISPLAY PANEL - 5 mg CARTON

PRINCIPAL DISPLAY PANEL - 10 mg BOTTLE LABEL

PRINCIPAL DISPLAY PANEL - 10 mg CARTON

PRINCIPAL DISPLAY PANEL - 15 mg BOTTLE LABEL



PRINCIPAL DISPLAY PANEL - 15 mg CARTON

DEXEDRINE SPANSULE

dextroamphetamine sulfate capsule, extended release

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:64896-673
Route of Administration	ORAL	**DEA Schedule**	CII

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
DEXTROAMPHETAMINE SULFATE (UNII: JJ768O327N) (DEXTROAMPHETAMINE - UNII:TZ47U051FI)	DEXTROAMPHETAMINE SULFATE	5 mg

Inactive Ingredients	
Ingredient Name	**Strength**
CETYL ALCOHOL (UNII: 936JST6JCN)	
D&C YELLOW NO. 10 (UNII: 35SW5USQ3G)	
DIBUTYL SEBACATE (UNII: 4W5IH7FLNY)	
ETHYLCELLULOSES (UNII: 7Z8S9VYZ4B)	
FD&C BLUE NO. 1 (UNII: H3R47K3TBD)	
FD&C RED NO. 40 (UNII: WZB9127XOA)	
FD&C YELLOW NO. 6 (UNII: H77VEI93A8)	
GELATIN (UNII: 2G86QN327L)	
HYPROMELLOSES (UNII: 3NXW29V3WO)	
POLYETHYLENE GLYCOL, UNSPECIFIED (UNII: 3WQ0SDW1A)	
POVIDONE (UNII: FZ989GH94E)	
SODIUM LAURYL SULFATE (UNII: 368GB5141J)	

Product Characteristics			
Color	brown (brown cap and natural body)	**Score**	no score
Shape	CAPSULE	**Size**	14mm
Flavor		**Imprint Code**	IX;5mg;673;5mg
Contains			

Packaging				
#	**Item Code**	**Package Description**	**Marketing Start Date**	**Marketing End Date**
1	NDC:64896-673-10	1 in 1 CARTON	08/02/1976	
1		90 in 1 BOTTLE; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NDA	NDA017078	08/02/1976	

DEXEDRINE SPANSULE

dextroamphetamine sulfate capsule, extended release

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:64896-674
Route of Administration	ORAL	**DEA Schedule**	CII

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
DEXTROAMPHETAMINE SULFATE (UNII: JJ768O327N) (DEXTROAMPHETAMINE - UNII:TZ47U051FI)	DEXTROAMPHETAMINE SULFATE	10 mg

Inactive Ingredients

Ingredient Name	Strength
CETYL ALCOHOL (UNII: 936JST6JCN)	
D&C YELLOW NO. 10 (UNII: 35SW5USQ3G)	
DIBUTYL SEBACATE (UNII: 4W5IH7FLNY)	
ETHYLCELLULOSES (UNII: 7Z8S9VYZ4B)	
FD&C BLUE NO. 1 (UNII: H3R47K3TBD)	
FD&C RED NO. 40 (UNII: WZB9127XOA)	
FD&C YELLOW NO. 6 (UNII: H77VEI93A8)	
GELATIN (UNII: 2G86QN327L)	
HYPROMELLOSES (UNII: 3NXW29V3WO)	
POLYETHYLENE GLYCOL, UNSPECIFIED (UNII: 3WQ0SDW1A)	
POVIDONE (UNII: FZ989GH94E)	
SODIUM LAURYL SULFATE (UNII: 368GB5141J)	

Product Characteristics

Color	brown (brown cap and natural body)	**Score**	no score
Shape	CAPSULE	**Size**	14mm
Flavor		**Imprint Code**	IX;10mg;674;10mg
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:64896-674-10	1 in 1 CARTON	08/02/1976	
1		90 in 1 BOTTLE; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NDA	NDA017078	08/02/1976	

DEXEDRINE SPANSULE

dextroamphetamine sulfate capsule, extended release

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:64896-675

Route of Administration	ORAL	DEA Schedule	CII

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
DEXTROAMPHETAMINE SULFATE (UNII: JJ768O327N) (DEXTROAMPHETAMINE - UNII:TZ47U051FI)	DEXTROAMPHETAMINE SULFATE	15 mg

Inactive Ingredients

Ingredient Name	Strength
CETYL ALCOHOL (UNII: 936JST6JCN)	
D&C YELLOW NO. 10 (UNII: 35SW5USQ3G)	
DIBUTYL SEBACATE (UNII: 4W5IH7FLNY)	
ETHYLCELLULOSES (UNII: 7Z8S9VYZ4B)	
FD&C BLUE NO. 1 (UNII: H3R47K3TBD)	
FD&C RED NO. 40 (UNII: WZB9127XOA)	
FD&C YELLOW NO. 6 (UNII: H77VEI93A8)	
GELATIN (UNII: 2G86QN327L)	
HYPROMELLOSES (UNII: 3NXW29V3WO)	
POLYETHYLENE GLYCOL, UNSPECIFIED (UNII: 3WQ0SDW1A)	
POVIDONE (UNII: FZ989GH94E)	
SODIUM LAURYL SULFATE (UNII: 368GB5141J)	

Product Characteristics

Color	brown (brown cap and natural body)	**Score**	no score
Shape	CAPSULE	**Size**	16mm
Flavor		**Imprint Code**	IX;15mg;675;15mg
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:64896-675-10	1 in 1 CARTON	08/02/1976	
1		90 in 1 BOTTLE; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NDA	NDA017078	08/02/1976	

Labeler - Amneal Pharmaceuticals LLC (123797875)

Establishment

Name	Address	ID/FEI	Business Operations
Amneal Pharmaceuticals of New York, LLC		123797875	pack(64896-673, 64896-674, 64896-675)

Establishment

Name	Address	ID/FEI	Business Operations
AndersonBrecon Inc.		053217022	pack(64896-673, 64896-674, 64896-675)

Establishment

Name	Address	ID/FEI	Business Operations
Cambrex Charles City, Inc.		782974257	api manufacture(64896-673, 64896-674, 64896-675)

Establishment

Name	Address	ID/FEI	Business Operations
Catalent Pharma Solutions, LLC		829672745	analysis(64896-673, 64896-674, 64896-675) , manufacture(64896-673, 64896-674, 64896-675)

Establishment

Name	Address	ID/FEI	Business Operations
Catalent Pharma Solutions, LLC		014167995	analysis(64896-673, 64896-674, 64896-675)