

Adderall (amphetamine)

FDA ALERT [02/2006] Sudden Unexplained Death, Cardiac/Cardiovascular, and Psychiatric Adverse Events Associated with Stimulant Therapy for ADHD.

In February of 2006, the FDA warned of serious cardiac and cardiovascular risks including sudden unexplained death (SUD) associated with the use of amphetamine or dextroamphetamine in children, adolescents and adults. Individuals with structural heart abnormalities are at a greater risk for these adverse cardiac/cardiovascular effects although those without structural cardiac abnormalities are also at risk. In addition, psychiatric adverse events including hallucinations, increased aggression and mania have been reported in individuals taking amphetamine and dextroamphetamine. The risk of these effects is greater in those with existing psychiatric illness.

Available as:

- Amphetamine sulfate (racemic amphetamine sulfate) – immediate release
 - Tablets: 5mg
- DextroStat[®] (dextroamphetamine) – immediate release
 - Tablets: 5mg, 10mg
- Dexedrine[®] (dextroamphetamine) – immediate release
 - Tablets: 5mg
- Dexedrine spansules[®] (dextroamphetamine) – sustained release
 - Capsules: 5mg, 10mg, 15mg
- Adderall[®] (mixed amphetamine salts) – immediate release
 - Tablets: 5mg, 7.5mg, 10mg, 12.5mg, 15mg, 20mg, 30mg
- Adderall XR[®] (mixed amphetamine salts) – extended release

- Capsules: 5mg, 10mg, 15mg, 20mg, 25mg, 30mg

What is amphetamine and what does it treat?

Amphetamine, dextroamphetamine, and mixed amphetamine salts are prescription medications that have been proven effective in the treatment of attention-deficit hyperactivity disorder (ADHD) in children, adolescents and adults. ADHD is associated with severe inattention, hyperactivity and impulsivity that interfere with an individual's ability to function in school, at work or in social settings. Examples of functionally impairing ADHD symptoms include making careless mistakes, losing things necessary for tasks, the inability to sit still and focus, and interrupting or intruding on others. Adults have similar symptoms but display less hyperactivity compared to children. Adults with ADHD may be more prone to procrastination, becoming easily frustrated and taking on many tasks at once while accomplishing none of them. A person may have severe inattention without hyperactivity or impulsivity and still meet criteria for a diagnosis of ADHD. A person with inattentive symptoms only can respond equally well to amphetamine or dextroamphetamine as someone who has inattentive and/or hyperactive and impulsive symptoms.

Amphetamine, dextroamphetamine, and mixed amphetamine salts increase effective use of dopamine and norepinephrine in parts of the brain that regulate attention and behavior in order to control symptoms associated with ADHD and improve functioning. Scientific literature shows that stimulant medications including amphetamine and dextroamphetamine are the most effective treatment options for ADHD. The American Academy of Pediatrics and the American Academy of Child and Adolescent Psychiatry consider these medicines to be the best treatment options. Behavioral interventions and lifestyle modifications are also useful.

What is the most important information I should know about amphetamine?

Amphetamine and dextroamphetamine should be avoided in individuals with psychotic symptoms caused by schizophrenia, schizoaffective disorder, bipolar disorder or any other brain disorder associated with psychotic symptoms because they are likely to worsen psychotic illness. These medications should also be avoided in people with a heart defect (structural abnormalities), uncontrolled high blood pressure, a disorder of the heart or blood vessels, overactive thyroid, glaucoma, uncontrolled seizure disorders, a history of drug abuse and in women who are pregnant or planning to become pregnant. Sudden unexplained death (SUD) has been associated with amphetamine abuse and it has been reported in children and adults with (and some without) underlying cardiac abnormalities taking recommended doses of amphetamines, including Adderall® and Adderall XR®. Adults taking amphetamine have higher rates of heart attack and stroke compared to those who do not take stimulants.

Amphetamine and dextroamphetamine should not be taken together with or within 14 days of taking a drug used to treat depression, called a Monoamine Oxidase Inhibitor (MAOI). MAOIs include Nardil (phenelzine), Parnate (tranylcypromine), Emsam (selegiline), and other brands. Coadministering amphetamine or dextroamphetamine

within 2 weeks of taking a MAOI can result in serious, sometimes fatal, reactions, including high body temperature, high blood pressure, seizures (convulsions) and rarely coma.

Amphetamine and dextroamphetamine are known to produce euphoria (feeling high), increased energy, and wakefulness, which carry a potential for abuse (using more than prescribed to feel high). This potential for abuse has caused amphetamine medications to become highly regulated in the United States. Pharmacies must closely regulate the storage and dispensing of these medications and in some states, physicians must write prescriptions for these medications on tamper-resistant prescription pads.

There are several studies showing effective ADHD treatment with stimulants may **prevent** an individual with ADHD from developing a substance abuse disorder due to “self-medicating” with alcohol, marijuana or other illicit drugs. The risk comes from **not** treating ADHD. If an individual has an active substance abuse disorder and is not motivated for recovery, amphetamine or dextroamphetamine is not the best treatment option and his/or her health care provider may recommend an alternative medication without abuse potential.

Are there specific concerns about amphetamine and pregnancy?

If you are planning on becoming pregnant, inform your healthcare provider immediately so that your healthcare provider can best manage your medications.

Amphetamine and dextroamphetamine have been shown to cause fetal malformation and death in mice when administered at a higher dose than that of human dose. One report shows severe congenital deformity in a baby born to a woman who took dextroamphetamine (and other medication) during the first trimester of pregnancy.

Infants born to mothers dependent on amphetamine or dextroamphetamine have an increased risk of premature delivery and low birth weight. These infants may also experience symptoms of withdrawal such as agitation and lack of energy.

Several case reports show that amphetamine use during pregnancy significantly influences development of exposed children up to at least 10 years old with an increase in aggressive behavior during fetal life.

Mothers taking amphetamine or dextroamphetamine should be advised to refrain from breast-feeding as amphetamine and dextroamphetamine are excreted in breast milk.

What should I discuss with my healthcare provider before taking amphetamine?

- Symptoms that are most bothersome to you about your condition
- Any medical problems, including heart disease, high blood pressure or mental illness
- Medications you have taken in the past to treat ADHD

- All other medications you are currently taking and any medication allergies you have
- Any medication side effects that you may have experienced in the past, or are currently experiencing
- If you are pregnant, plan to become pregnant, or are breast-feeding
- If you drink alcohol or use illicit drugs.

How should I take amphetamine?

Amphetamine medications are taken by mouth, in the morning, with or without food, exactly as prescribed by your healthcare professional.

Although all forms of amphetamine and dextroamphetamine dissolve in the stomach to give the same active medication, there are some differences between each form. Different forms are available for this medication for several reasons: 1) for easier swallowing, 2) for fewer side effects, and 3) for taking this medicine fewer times each day.

- Tablets: Swallow the tablets whole. Chewing the tablets gives an unpleasant taste and can be irritating to the mouth and throat. Take it 1-3 times daily as instructed by your doctor.
- Sprinkle capsules (Dexedrine Spansule®): May be swallowed whole or opened and sprinkled onto food like applesauce or pudding. Sprinkle capsules should not be chewed. Take once daily as per your doctor's instructions.
- Long acting capsules (Adderall XR®, and Dexedrine Spansule®) can be taken once daily. Do not cut, crush, or chew.

What happens if I miss a dose of amphetamine?

If you miss a dose of amphetamine, take it as soon as you remember if it is not too close to when your next dose is due - discuss this with your healthcare provider. If it is close to your next dose, wait until then to take the medication and skip the missed dose. Do not double your next dose or take more than what you have been told to take.

What should I avoid while taking amphetamine?

You should not drink alcohol or use illegal drugs while taking amphetamine, dextroamphetamine, or mixed amphetamine salts.

The absorption of amphetamine medications can be reduced if strong organic acids are present in the stomach at the time of taking amphetamine medications. The following foods should be avoided for 1 hour before and after taking an amphetamine medication: citrus fruit, citrus juices, sodas/carbonated beverages, lemonade, Gatorade, vitamins/food and food supplements containing vitamin C.

What happens if I overdose with amphetamine?

If an overdose occurs, whether intentional or accidental, immediate medical attention is necessary. Call your doctor or emergency medical service (911).

Overdosing with amphetamine may lead to high body temperature, abnormal heart rhythms, excessively high blood pressure, seizures, coma, and death.

What are the possible side effects of amphetamine?

Upset stomach, loss of appetite and insomnia are the most common side effects associated with the use of amphetamine medications.

- Upset stomach can be managed by taking the medicine on a full stomach or lowering the dose.
- Loss of appetite and weight loss can be improved by serving the child his or her favorite foods when stimulant effects are low (for example in the morning before medication or at night when the medication effects are less), or use nutritional supplements.
- Insomnia can be improved by giving the medication as early in the day as possible, avoiding afternoon or evening dosing. Some clinicians will prescribe sedating medications like clonidine, guanfacine, or trazodone at night. Melatonin has also been found effective to manage insomnia associated with ADHD medication.
- Abnormal involuntary movements or muscle twitches called tics (for example, excessive eye-blinking, nose scrunching, or shoulder shrugging) can be associated with amphetamines. If this occurs, the dose of medication should be lowered or the medication should be changed.
- Mild anxiety or restlessness can be managed with dosage reduction or changing medication.
- Misuse of amphetamine medications may cause sudden death and serious cardiovascular adverse events. Amphetamine medications should be avoided in individuals who have a heart defect (structural abnormalities), uncontrolled high blood pressure, or a disorder of the heart or blood vessels.
- Amphetamine medications are rarely associated with clinically significant increases in blood pressure or heart rate. Blood pressure and heart rate should be monitored before starting medication, and then weekly while adjusting the dose and then every month to three months or when side effects like “racing heart”, shortness of breath or exercise fatigue becomes problematic.
- Severe anxiety, panic attacks, mania, hallucinations, paranoia and delusions are all possible. If they occur, the medication should be discontinued, and the individual should be evaluated by their health care provider.

Are there any risks for taking amphetamine for long periods of time?

Although treatment with amphetamine medications can lead to mild growth suppression, many studies have shown that this deficit in growth is small, attenuates with time, and should not be a clinical concern for most children treated with amphetamine medications. Height, weight, and eating habits should be assessed before starting medication and regularly thereafter. If a child's growth is thought to be affected, the risk versus benefit of taking time off medication to allow for growth acceleration should be considered.

What other drugs may interact with this medication?

- Medications used to treat depression such as Tricyclic antidepressants (TCA) and monoamine oxidase inhibitors (MAOI) can interact with amphetamine resulting in serious reactions including high body temperature, high blood pressure, and seizures (convulsions). Tell your healthcare provider if you are beginning or have recently discontinued any of these medications.
- Medications that may increase the effects and adverse effects of amphetamine, dextroamphetamine and mixed amphetamine salts include:
 - Atomoxetine (Strattera®), sibutramine (Meridia®), phenylephrine, guarana, and caffeine.
 - Fluoxetine (Prozac®), paroxetine (Paxil®), bupropion (Wellbutrin®), venlafaxine (Effexor®)
- Amphetamine, dextroamphetamine or mixed amphetamine salts may increase the blood level of some seizure medications such as Phenobarbital or phenytoin. If you are taking any of these medications with amphetamine medication, tell your healthcare provider immediately.
- Amphetamine, dextroamphetamine or mixed amphetamine salts may inhibit antihypertensive response to some blood pressure medications such as clonidine, guanethidine and guanadrel. Tell your healthcare provider immediately if you are taking any of these medications with amphetamine medication.
- Antacids may increase amphetamine effects. Consult with your healthcare provider before consuming antacids while taking amphetamine medication.
- Urinary alkalinizers (bicarbonate) may increase the effects of amphetamine, while urinary acidifiers (citrus beverages) may decrease the effects of amphetamine. Consult with your healthcare provider before starting any medications/food/food supplements that can alkalinize or acidify the urine while taking amphetamine medication.

How long does it take for amphetamine to work?

Amphetamine medications start working within 1-3 hours of ingesting the medications. The effect generally lasts about 4-5 hours for the immediate-release forms and 8-12 hours for the sustained release forms.

*Updated by Jane Tran Tesoro, Pharm.D., BCPP
March 2007*



NAMI wishes to thank the College of Psychiatric and Neurological Pharmacists for producing this fact sheet.