Brand Names

Adderall, Adderall XR, Mydayis

Indication Specific Dosing

For the treatment of attention-deficit hyperactivity disorder (ADHD)

Oral dosage (immediate-release)

Adults weighing more than 50 kg†

5 mg PO once or twice daily, initially. May increase the dose by 5 mg/day at weekly intervals based on clinical response. Usual Max: 40 mg/day. Doses more than 40 mg/day are rarely needed. Coadministration of certain drugs may need to be avoided or dosage adjustments may be necessary; review drug interactions.

Adults weighing 50 kg or less†

5 mg PO once or twice daily, initially. May increase the dose by 5 mg/day at weekly intervals based on clinical response. Usual Max: 40 mg/day. Doses more than 40 mg/day are rarely needed. Coadministration of certain drugs may need to be avoided or dosage adjustments may be necessary; review drug interactions.

Children and Adolescents 6 to 17 years weighing more than 50 kg

5 mg PO once or twice daily, initially. May increase the dose by 5 mg/day at weekly intervals based on clinical response. However, a maximum dose of 60 mg/day may be considered. Use the lowest effective dose. Coadministration of certain drugs may need to be avoided or dosage adjustments may be necessary; review drug interactions.

Children and Adolescents 6 to 17 years weighing 50 kg or less

5 mg PO once or twice daily, initially. May increase the dose by 5 mg/day at

weekly intervals based on clinical response. Usual Max: 40 mg/day. Doses more than 40 mg/day are rarely needed. Use the lowest effective dose. Coadministration of certain drugs may need to be avoided or dosage adjustments may be necessary; review drug interactions.

Children 3 to 5 years

2.5 mg PO once daily in the morning, initially. May increase the dose by 2.5 mg/day at weekly intervals based on clinical response. Usual Max: 40 mg/day. Coadministration of certain drugs may need to be avoided or dosage adjustments may be necessary; review drug interactions. The American Academy of Pediatrics (AAP) does not recommend the use of dextroamphetamine in this age group due to lack of safety and efficacy data.

Oral dosage (extended-release; i.e., Adderall XR)

Adults

20 mg PO once daily in the morning. In clinical trials, titration doses were allowed up to 60 mg/day; however, there was no consistent evidence that doses above 20 mg/day conferred additional benefit. Persons taking divided doses of immediate-release amphetamine; dextroamphetamine (e.g., twice daily), may be switched to extended-release amphetamine; dextroamphetamine at the same total daily dose taken once daily. Use the lowest effective dose. Coadministration of certain drugs may need to be avoided or dosage adjustments may be necessary; review drug interactions.

Adolescents

10 mg PO once daily in the morning, initially. May increase the dose to 20 mg/day after 1 week based on clinical response. In clinical trials, titration doses were allowed up to 40 mg/day for weight 75 kg or less and from 50 to 60 mg/day for weight more than 75 kg; however, there was no consistent evidence that doses above 20 mg/day conferred additional benefit. Persons taking divided doses of immediate-release amphetamine; dextroamphetamine (e.g., twice daily), may be switched to extended-release amphetamine; dextroamphetamine at the same total daily dose taken once daily. Use the lowest effective dose. Coadministration of certain drugs may need to be avoided or dosage adjustments may be necessary; review drug interactions.

Children 6 to 12 years

5 to 10 mg PO once daily in the morning, initially. May increase the dose by 5 to 10 mg/day at weekly intervals based on clinical response. Max: 30 mg/day. Persons taking divided doses of immediate-release amphetamine; dextroamphetamine (e.g., twice daily), may be switched to extended-release amphetamine; dextroamphetamine at the same total daily dose taken once daily. Use the lowest effective dose. Coadministration of certain drugs may need to be avoided or dosage adjustments may be necessary; review drug interactions.

Oral dosage (extended-release; i.e., Mydayis)

Adults

12.5 mg PO once daily in the morning, initially; an initial dose of 25 mg PO once daily may be considered for some. May increase the dose by 12.5 mg/day at weekly intervals based on clinical response. Max: 50 mg/day. Doses more than 50 mg/day have not shown additional clinically meaningful benefit. Use the lowest effective dose. For patients switching from another medication or amphetamine product, discontinue that treatment, and titrate using the titration schedule. Do not substitute for other amphetamine products on a milligram-per-milligram basis because of different amphetamine base compositions and differing pharmacokinetic profiles. Coadministration of certain drugs may need to be avoided or dosage adjustments may be necessary; review drug interactions.

Adolescents 13 to 17 years

12.5 mg PO once daily in the morning, initially. May increase the dose by 12.5 mg/day at weekly intervals based on clinical response. Max: 25 mg/day. Use the lowest effective dose. For patients switching from another medication or amphetamine product, discontinue that treatment, and titrate using the titration schedule. Do not substitute for other amphetamine products on a milligram-per-milligram basis because of different amphetamine base compositions and differing pharmacokinetic profiles. Coadministration of certain drugs may need to be avoided or dosage adjustments may be necessary; review drug interactions.

For the treatment of narcolepsy

Oral dosage (immediate-release)

Adults

5 to 60 mg/day PO in 2 or 3 divided doses.

Children and Adolescents 12 to 17 years

10 mg/day PO in 1 to 3 divided doses, initially. May increase the dose by 10 mg/day at weekly intervals based on clinical response and tolerability. Max: 60 mg/day.

Children 6 to 11 years

5 mg/day PO in 1 to 3 divided doses, initially. May increase the dose by 5 mg/day at weekly intervals based on clinical response and tolerability. Max: 60 mg/day.

For the treatment of cocaine dependence†

For treatment as monotherapy†

Oral dosage (extended-release capsules)

Adults

Usual dose: 60 to 80 mg/day. Some data indicate patients may require dosing at or above the FDA-labeled max dose for ADHD in order to effectively reduce cocaine use (low certainty, conditional recommendation). A meta-analysis indicated that psychostimulant medications, including extended-release mixed amphetamine salts (ER-MAS), were associated with better cocaine-related outcomes, including sustained abstinence and cocaine-negative urine screen results. However, no difference was noted in treatment retention. ER-MAS may be particularly helpful in individuals with comorbid ADHD to assist with treatment of both conditions simultaneously. Results of a randomized, placebo-controlled trial in adults with cocaine use disorder and concomitant ADHD showed that patients receiving ER-MAS had significant improvement in ADHD symptom severity as well as reduced cocaine use and improved rates of continuous abstinence vs. placebo. One guideline suggests that the use of psychostimulants for this indication be limited to specialists who are board certified in addiction medicine, addiction psychiatry, or commensurate training and competency.

For treatment in combination with topiramate†

Oral dosage (extended-release capsules)

Adults

Doses up to 60 mg/day, given along with topiramate therapy, have been used. Some data indicate patients may require dosing at or above the FDA-labeled max dose for ADHD in order to effectively reduce cocaine use (low certainty, conditional recommendation). The extended-release mixed amphetamine salts (ER-MAS) in combination with topiramate may be helpful for reducing cocaine cravings and achieving cocaine abstinence. A meta-analysis found the combination had positive effects in establishing a period of cocaine abstinence when compared to placebo treatment. Additionally, a randomized controlled trial demonstrated that cocaine cravings decreased more quickly with combination treatment vs. placebo. These effects may be even more pronounced in patients with frequent cocaine use. This combination may be helpful for patients with comorbid ADHD or alcohol use disorder, as topiramate has shown benefit in reducing alcohol consumption. One guideline suggests that the use of psychostimulants for this indication be limited to specialists who are board certified in addiction medicine, addiction psychiatry, or commensurate training and competency.

Contraindications And Precaution

Drug Interactions

The coadministration of certain medications may lead to harm and require avoidance or therapy modification; review all drug interactions prior to concomitant use of other medications.

Hypersensitivity

This medication is contraindicated in patients with a history of hypersensitivity to it or any of its components.

substance abuse disorder

Central nervous system (CNS) stimulants, such as amphetamine; dextroamphetamine mixed salts, have a high potential for abuse and misuse, which can lead to the development of a substance abuse disorder, including addiction. Assess each individual's risk for substance abuse (including alcoholism), misuse, or addiction before prescribing a CNS stimulant, and monitor for the development of these behaviors or conditions throughout treatment. Children and adolescents with attention-deficit hyperactivity disorder (ADHD) are more prone to substance abuse compared to those without ADHD, and those with co-occurring mental health conditions (e.g., depression, disruptive behavior disorders) are at even greater risk; however, appropriate treatment of ADHD with medication and behavior therapy may reduce the risk of developing a

substance abuse disorder. Prescribing and dispensing the smallest appropriate quantity may help to minimize abuse, misuse, and overdosage. CNS stimulants can be diverted for non-medical use into illicit channels or distribution. The most common source of non-medical use is sharing from family or friends with misuse of the individual's own prescription or obtaining from illicit channels occurring less frequently. Sharing of CNS stimulant medications can lead to substance abuse disorder and addiction in those they are shared with. Misuse and abuse of CNS stimulants can result in potential for overdose or poisoning and death; the risk is increased with higher doses or unapproved methods of administration, such as snorting or injection. Educate individuals and their families about these risks, proper storage, and proper disposal of any unused medication. Misuse or abuse 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 stimulant abuse or misuse.

mood disorder, psychotic disorder, suicidal ideation

CNS stimulants should be used with caution in those with bipolar disorder or a pre-existing psychotic disorder (e.g., schizophrenia). CNS stimulants may exacerbate symptoms of behavior disturbance and thought disorder in individuals with pre-existing psychosis. These medications can also induce mania or a mixed episode in individuals with bipolar disorder. Prior to initiating treatment with amphetamine; dextroamphetamine, screen individuals for risk factors for bipolar disorder or developing an episode of mania (e.g., mood disorder, comorbid or history of depressive symptoms or a family history of suicide, bipolar disorder, or depression). At recommended doses, CNS stimulants may also cause psychotic or manic symptoms (such as hallucinations, delusions, or mania) in individuals without a prior history of psychosis or mania. Advise individuals and their caregivers to promptly report suicidal ideation or any changes in mood or behavior and consider discontinuing treatment if these symptoms occur.

cardiac disease, family history of sudden cardiac death

Sudden death has been reported in individuals with structural cardiac abnormalities or other serious cardiac disease who were treated with CNS stimulants at the recommended ADHD dosages. Avoid use of CNS stimulants in individuals with known structural cardiac abnormalities, cardiomyopathy, serious cardiac arrhythmias, coronary artery disease, or other serious cardiac disease. Prior to initiating any CNS stimulant, carefully assess patient for the presence of cardiac disease (i.e., perform a careful patient history, assess for any family history of sudden cardiac death or ventricular

arrhythmia, and complete a physical exam) and counsel individuals to report symptoms of cardiac disease (i.e., exertional chest pain, unexplained syncope) immediately. Although it is reasonable for a health care provider to obtain an ECG as part of the cardiovascular evaluation, it is not mandatory. Treatment with stimulant products should not be withheld because an ECG is not performed. However, any individual with significant findings on physical examination, ECG, or from patient or family history (such as known congenital heart disease, structural heart disease, arrhythmias, or a family history of sudden cardiac death in members younger than 35 years of age) should be referred for consultation with a pediatric cardiologist prior to starting the stimulant medication. Overall, studies have not shown an association between the use of ADHD medications and adverse cardiovascular events; however, long-term cardiovascular risks associated with ADHD medications are unknown. CNS stimulant medications, including amphetamine; dextroamphetamine, can cause an increase in blood pressure (mean increase approximately 2 to 4 mmHg) and heart rate (mean increase approximately 3 to 6 beats per minute). Some individuals may have larger increases. Monitor all individuals receiving amphetamine; dextroamphetamine for hypertension and tachycardia. Careful monitoring should be performed after initiation of stimulant medications; if any abnormal findings or arrhythmias are diagnosed during treatment, consider discontinuation of the stimulant.

children

Extended-release amphetamine; dextroamphetamine is not recommended for use in children younger than 6 years due to higher medication exposure and increased adverse reactions. An FDA analysis reported children younger than 6 years receiving extended-release stimulants have higher adverse reaction rates, particularly significant weight loss, compared to older children on the same dose. For children younger than 6 years who experience weight loss or other adverse reactions while receiving extended-release stimulants, consider discontinuing the medication or switching to an alternative, such as an immediate-release stimulant. Monitor growth and development and provide necessary interventions to minimize weight loss.

tics, Tourette's syndrome

CNS stimulants, including amphetamine; dextroamphetamine products, have been associated with the onset or exacerbation of motor and verbal tics. Worsening of Tourette syndrome has also been reported. Prior to initiating amphetamine; dextroamphetamine, carefully assess family history and clinically evaluate individuals for motor or verbal tics or Tourette syndrome. Regularly monitor amphetamine; dextroamphetamine-treated individuals for the emergence or worsening of tics or Tourette syndrome and discontinue treatment if clinically appropriate.

geriatric

Geriatric adults or debilitated individuals may be more susceptible to the CNS and sympathomimetic side effects of the amphetamines; use with caution in the older adult. Medication should be titrated with low doses initially and with a slow increase.

renal failure, renal impairment

Use amphetamine; dextroamphetamine with caution in individuals with renal impairment or renal failure. Amphetamine; dextroamphetamine extended-release product dosages should be reduced in individuals with an eGFR less than 30 mL/minute/1.73 m2, and use of these dosage forms in individuals with renal failure (end-stage renal disease) is not recommended.

pregnancy

Available data on the use of prescription amphetamines during human pregnancy have not identified a drug-associated risk of major birth defects and miscarriage. Infants born to individuals taking amphetamines during pregnancy have an increased risk of premature delivery and low birth weight. Amphetamines cause vasoconstriction and may decrease placental perfusion. In addition, amphetamines can stimulate uterine contractions, increasing the risk of premature delivery. Much of the historical data on amphetamine use during pregnancy is derived from studies of illicit use, which may be complicated by comorbid substance abuse or ingestion of higher-than-prescribed doses. These studies report increased incidence of premature birth, low birth weight and length, lower occipitofrontal circumference, and neonatal withdrawal symptoms (e.g., abnormal sleep patterns, poor feeding, tremor, agitation, fatigue, hypertonia). However, more recent data demonstrate that risks associated with the use of prescription amphetamines may be lower than initially thought. Among 671 mother-child pairs enrolled in the Collaborative Perinatal Project who had first trimester exposure to amphetamines and 1,898 mother-child pairs with amphetamine exposures at any time during pregnancy, there was no evidence suggesting a relationship to large categories of major or minor malformations. Similarly, a large cohort study of pregnancy outcomes in the United States and 5 Nordic countries were compared to assess for the risks of major congenital malformations and cardiac effects in infants exposed to stimulants in utero. Of the 5,571 pregnant people who filled a prescription for amphetamines during the first trimester, 253 (4.54%) were diagnosed with malformations. In infants who were not exposed, 62,966 (3.5%) of the nearly 1.8 million infants developed malformations. After adjusting for underlying psychiatric disorders and other potential confounders, no increased risks were observed for amphetamine use compared to controls. Animal

studies identify long-term neurochemical and behavioral effects in offspring at clinically relevant amphetamine doses. A large cohort study evaluated stimulant use in the second half of pregnancy in 4,693 amphetamine/dextroamphetamine and 786 methylphenidate-exposed pregnancies compared to 2,496,711 unexposed pregnancies. This study found exposure to these medications in utero did not increase the risk of childhood neurodevelopmental disorders after adjustment for confounders, such as demographic characteristics and maternal ADHD or mental health diagnoses. There is a pregnancy exposure registry that monitors outcomes in pregnant people exposed to ADHD medications. Care teams are encouraged to register patients at https://womensmentalhealth.org/research/pregnancyregistry/adhd-medications/ or by calling 1-866-961-2388.

peripheral vasoconstriction or ischemia

Stimulant medications are associated with peripheral vasoconstriction or ischemia, including Raynaud phenomenon. Worsening of peripheral vascular disease is possible. Effects on circulation have been observed with therapeutic doses at different times throughout therapy in all age groups. Signs and symptoms are usually intermittent and mild and generally improve after reduction in dose or discontinuation of the drug. However, very rare sequelae include digital skin ulcer and/or soft tissue breakdown. Carefully monitor all individuals for digital changes during treatment with stimulant medications, especially those with pre-existing circulation problems. Instruct individuals to seek immediate medical attention if any new digital numbness, pain, skin discoloration, or temperature sensitivity occur, or if unexplained wounds appear on their fingers or toes. Further clinical evaluation (e.g., rheumatology referral) may be appropriate for individuals taking stimulants who develop signs or symptoms of peripheral vasculopathy.

neonates and infants exposed to this medication in utero

Neonates and infants exposed to this medication in utero are at risk for withdrawal symptoms after delivery. Monitor neonates and infants for symptoms of withdrawal such as feeding difficulties, irritability, agitation, and excessive drowsiness.

breast-feeding

Use amphetamine; dextroamphetamine with caution during breast-feeding. FDA-approved product labeling does not recommend breast-feeding in individuals taking amphetamines. However, some experts state that therapeutic dosages can be used during lactation with close monitoring of the child for irritability, insomnia, and poor feeding. Limited data suggest that at typical doses prescribed for medical indications,

amphetamines do not cause infant adverse effects. However, the long-term neurodevelopmental effects on infants are unknown. Dextroamphetamine is present in human milk in small amounts. Limited data indicate a relative infant dose of 2.46% to 7.25% of the maternal weight-adjusted dosage, with a milk to plasma ratio between 2 and 5.2. Large dosages of amphetamines may interfere with milk production, especially in people without well established lactation. Methylphenidate, dexmethylphenidate, and serdexmethylphenidate/methylphenidate are alternative options for treatment of ADHD in the breast-feeding individual, as limited data indicates that methylphenidate levels in milk are very low and not detectable in infant serum.

Pregnancy And Lactation

Available data on the use of prescription amphetamines during human pregnancy have not identified a drug-associated risk of major birth defects and miscarriage. Infants born to individuals taking amphetamines during pregnancy have an increased risk of premature delivery and low birth weight. Amphetamines cause vasoconstriction and may decrease placental perfusion. In addition, amphetamines can stimulate uterine contractions, increasing the risk of premature delivery. Much of the historical data on amphetamine use during pregnancy is derived from studies of illicit use, which may be complicated by comorbid substance abuse or ingestion of higher-than-prescribed doses. These studies report increased incidence of premature birth, low birth weight and length, lower occipitofrontal circumference, and neonatal withdrawal symptoms (e.g., abnormal sleep patterns, poor feeding, tremor, agitation, fatigue, hypertonia). However, more recent data demonstrate that risks associated with the use of prescription amphetamines may be lower than initially thought. Among 671 mother-child pairs enrolled in the Collaborative Perinatal Project who had first trimester exposure to amphetamines and 1,898 mother-child pairs with amphetamine exposures at any time during pregnancy, there was no evidence suggesting a relationship to large categories of major or minor malformations. Similarly, a large cohort study of pregnancy outcomes in the United States and 5 Nordic countries were compared to assess for the risks of major congenital malformations and cardiac effects in infants exposed to stimulants in utero. Of the 5,571 pregnant people who filled a prescription for amphetamines during the first trimester, 253 (4.54%) were diagnosed with malformations. In infants who were not exposed, 62,966 (3.5%) of the nearly 1.8 million infants developed malformations. After adjusting for underlying psychiatric disorders and other potential confounders, no increased risks were observed for amphetamine use compared to controls. Animal studies identify long-term neurochemical and behavioral effects in offspring at clinically relevant amphetamine doses. A large cohort study evaluated stimulant use in the second half of pregnancy in 4,693 amphetamine/dextroamphetamine and 786 methylphenidate-exposed pregnancies compared to 2,496,711 unexposed pregnancies.

This study found exposure to these medications in utero did not increase the risk of childhood neurodevelopmental disorders after adjustment for confounders, such as demographic characteristics and maternal ADHD or mental health diagnoses. There is a pregnancy exposure registry that monitors outcomes in pregnant people exposed to ADHD medications. Care teams are encouraged to register patients at https://womensmentalhealth.org/research/pregnancyregistry/adhd-medications/ or by calling 1-866-961-2388.

Interactions

Acarbose: (Moderate) Sympathomimetic agents and adrenergic agonists tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when pseudoephedrine, phenylephrine, and other sympathomimetics are administered to patients taking antidiabetic agents. Epinephrine and other sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.
Acebutolol: (Moderate) Monitor hemodynamic parameters and for loss of efficacy during concomitant sympathomimetic agent and beta-blocker use; dosage adjustments may be necessary. Concomitant use may antagonize the cardiovascular effects of either drug.
Acetaminophen; Aspirin, ASA; Caffeine: (Moderate) Avoid excessive caffeine intake during use of the amphetamine salts. Caffeine is a CNS-stimulant and such actions are expected to be additive when coadministered with other CNS stimulants or psychostimulants. Excessive caffeine ingestion (via medicines, foods like chocolate, dietary supplements, or beverages including coffee, green tea, other teas, colas) may contribute to side effects like nervousness, irritability, nausea, insomnia, or tremor. Patients should avoid medications and dietary supplements which contain high amounts of caffeine.
Acetaminophen; Aspirin, ASA; Caffeine: (Moderate) Avoid excessive caffeine intake during use of the amphetamine salts. Caffeine is a CNS-stimulant and such actions are expected to be additive when coadministered with other CNS stimulants or psychostimulants. Excessive caffeine ingestion (via medicines, foods like chocolate, dietary supplements, or beverages including coffee, green tea, other teas, colas) may contribute to side effects like nervousness, irritability, nausea, insomnia, or tremor. Patients should avoid medications and dietary supplements which contain high amounts of caffeine.
Acetaminophen; Aspirin; diphenhydrAMINE: (Moderate) Amphetamines may pharmacodynamically counteract the sedative properties of some antihistamines, such

as the sedating H1-blockers (i.e., diphenhydramine). This effect may be clinically important if a patient is receiving an antihistamine agent for treatment of insomnia. Alternatively, if a patient is receiving an amphetamine for treatment of narcolepsy, the combination with a sedating antihistamine may reverse the action of the amphetamine.
Acetaminophen; Caffeine: (Moderate) Avoid excessive caffeine intake during use of the amphetamine salts. Caffeine is a CNS-stimulant and such actions are expected to be additive when coadministered with other CNS stimulants or psychostimulants. Excessive caffeine ingestion (via medicines, foods like chocolate, dietary supplements, or beverages including coffee, green tea, other teas, colas) may contribute to side effects like nervousness, irritability, nausea, insomnia, or tremor. Patients should avoid medications and dietary supplements which contain high amounts of caffeine.
Acetaminophen; Caffeine; Dihydrocodeine: (Moderate) Avoid excessive caffeine intake during use of the amphetamine salts. Caffeine is a CNS-stimulant and such actions are expected to be additive when coadministered with other CNS stimulants or psychostimulants. Excessive caffeine ingestion (via medicines, foods like chocolate, dietary supplements, or beverages including coffee, green tea, other teas, colas) may contribute to side effects like nervousness, irritability, nausea, insomnia, or tremor. Patients should avoid medications and dietary supplements which contain high amounts of caffeine.
Acetaminophen; Caffeine; Pyrilamine: (Moderate) Amphetamines may pharmacodynamically counteract the sedative properties of some antihistamines, such as the sedating H1-blockers (i.e., diphenhydramine). This effect may be clinically important if a patient is receiving an antihistamine agent for treatment of insomnia. Alternatively, if a patient is receiving an amphetamine for treatment of narcolepsy, the combination with a sedating antihistamine may reverse the action of the amphetamine. (Moderate) Avoid excessive caffeine intake during use of the amphetamine salts. Caffeine is a CNS-stimulant and such actions are expected to be additive when coadministered with other CNS stimulants or psychostimulants. Excessive caffeine ingestion (via medicines, foods like chocolate, dietary supplements, or beverages including coffee, green tea, other teas, colas) may contribute to side effects like nervousness, irritability, nausea, insomnia, or tremor. Patients should avoid medications and dietary supplements which contain high amounts of caffeine.
Acetaminophen; Chlorpheniramine: (Moderate) Amphetamines may pharmacodynamically counteract the sedative properties of some antihistamines, such as the sedating H1-blockers (i.e., diphenhydramine). This effect may be clinically important if a patient is receiving an antihistamine agent for treatment of insomnia. Alternatively, if a patient is receiving an amphetamine for treatment of narcolepsy, the combination with a sedating antihistamine may reverse the action of the amphetamine.
Acetaminophen; Chlorpheniramine; Dextromethorphan: (Moderate) Amphetamines may pharmacodynamically counteract the sedative properties of some antihistamines, such

as the sedating H1-blockers (i.e., diphenhydramine). This effect may be clinically important if a patient is receiving an antihistamine agent for treatment of insomnia. Alternatively, if a patient is receiving an amphetamine for treatment of narcolepsy, the combination with a sedating antihistamine may reverse the action of the amphetamine.
Acetaminophen; Chlorpheniramine; Dextromethorphan; Phenylephrine: (Moderate) Amphetamines may pharmacodynamically counteract the sedative properties of some antihistamines, such as the sedating H1-blockers (i.e., diphenhydramine). This effect may be clinically important if a patient is receiving an antihistamine agent for treatment of insomnia. Alternatively, if a patient is receiving an amphetamine for treatment of narcolepsy, the combination with a sedating antihistamine may reverse the action of the amphetamine.
Acetaminophen; Chlorpheniramine; Dextromethorphan; Pseudoephedrine: (Moderate) Amphetamines may pharmacodynamically counteract the sedative properties of some antihistamines, such as the sedating H1-blockers (i.e., diphenhydramine). This effect may be clinically important if a patient is receiving an antihistamine agent for treatment of insomnia. Alternatively, if a patient is receiving an amphetamine for treatment of narcolepsy, the combination with a sedating antihistamine may reverse the action of the amphetamine.
Acetaminophen; Chlorpheniramine; Phenylephrine : (Moderate) Amphetamines may pharmacodynamically counteract the sedative properties of some antihistamines, such as the sedating H1-blockers (i.e., diphenhydramine). This effect may be clinically important if a patient is receiving an antihistamine agent for treatment of insomnia. Alternatively, if a patient is receiving an amphetamine for treatment of narcolepsy, the combination with a sedating antihistamine may reverse the action of the amphetamine.
Acetaminophen; Codeine: (Moderate) If concomitant use of codeine and amphetamines is warranted, monitor patients for the emergence of serotonin syndrome. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs. The concomitant use of opioids with other drugs that affect the serotonergic neurotransmitter system has resulted in serotonin syndrome.
Acetaminophen; Dextromethorphan; Doxylamine: (Moderate) Amphetamines may pharmacodynamically counteract the sedative properties of some antihistamines, such as the sedating H1-blockers (i.e., diphenhydramine). This effect may be clinically important if a patient is receiving an antihistamine agent for treatment of insomnia. Alternatively, if a patient is receiving an amphetamine for treatment of narcolepsy, the combination with a sedating antihistamine may reverse the action of the amphetamine.
Acetaminophen; diphenhydrAMINE: (Moderate) Amphetamines may pharmacodynamically counteract the sedative properties of some antihistamines, such as the sedating H1-blockers (i.e., diphenhydramine). This effect may be clinically important if a patient is receiving an antihistamine agent for treatment of insomnia. Alternatively, if a patient is receiving an amphetamine for treatment of narcolepsy, the

combination with a sedating antihistamine may reverse the action of the amphetamine.
Acetaminophen; HYDROcodone: (Moderate) If concomitant use of hydrocodone and amphetamines is warranted, monitor patients for the emergence of serotonin syndrome. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs. The concomitant use of opioids with other drugs that affect the serotonergic neurotransmitter system has resulted in serotonin syndrome.
Acetaminophen; oxyCODONE: (Moderate) If concomitant use of oxycodone and amphetamines is warranted, monitor patients for the emergence of serotonin syndrome. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs. The concomitant use of opioids with other drugs that affect the serotonergic neurotransmitter system has resulted in serotonin syndrome.
Acetaminophen; Pamabrom; Pyrilamine: (Moderate) Amphetamines may pharmacodynamically counteract the sedative properties of some antihistamines, such as the sedating H1-blockers (i.e., diphenhydramine). This effect may be clinically important if a patient is receiving an antihistamine agent for treatment of insomnia. Alternatively, if a patient is receiving an amphetamine for treatment of narcolepsy, the combination with a sedating antihistamine may reverse the action of the amphetamine.
acetaZOLAMIDE: (Moderate) Monitor for an increase in the incidence and severity of amphetamine-related adverse effects during concomitant use of urinary alkalinizing agents. Increasing urine pH may increase amphetamine exposure by reducing urinary excretion of amphetamine. A urine pH more than 7.5 has been observed to increase the half-life of amphetamine from 8 to 10.5 hours to 16 to 31 hours when compared to a pH less than 6. Additionally, a urine pH more than 8 has been observed to reduce the amount of amphetamine excreted in the urine over 16 hours to less than 3% of the original dose; a 5-fold reduction compared to controls.
Aclidinium; Formoterol: (Moderate) Monitor blood pressure and heart rate during concomitant amphetamine; dextroamphetamine and formoterol use. Concomitant use may potentiate sympathetic effects.
Albuterol: (Moderate) Monitor blood pressure and heart rate during concomitant albuterol and amphetamine; dextroamphetamine use. Concomitant use may potentiate sympathetic effects.
Albuterol; Budesonide: (Moderate) Monitor blood pressure and heart rate during concomitant albuterol and amphetamine; dextroamphetamine use. Concomitant use may potentiate sympathetic effects.
ALFentanil: (Moderate) Because of the potential risk and severity of serotonin syndrome, caution should be observed when administering alfentanil with amphetamines. Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome particularly during treatment initiation and dose adjustment. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs.

Aliskiren; hydroCHLOROthiazide, HCTZ: (Minor) Amphetamines may counteract the activity of some antihypertensive agents, such as thiazide diuretics. Close monitoring of blood pressure is advised. Thiazide diuretics may also increase and prolong the actions of amphetamines by increasing the urinary pH.
Alkalinizing Agents: (Moderate) Monitor for an increase in the incidence and severity of amphetamine-related adverse effects during concomitant use of urinary alkalinizing agents. Increasing urine pH may increase amphetamine exposure by reducing urinary excretion of amphetamine. A urine pH more than 7.5 has been observed to increase the half-life of amphetamine from 8 to 10.5 hours to 16 to 31 hours when compared to a pH less than 6. Additionally, a urine pH more than 8 has been observed to reduce the amount of amphetamine excreted in the urine over 16 hours to less than 3% of the original dose; a 5-fold reduction compared to controls.
Almotriptan: (Moderate) Monitor for signs and symptoms of serotonin syndrome, particularly during treatment initiation and dosage increase, during concomitant serotonin-receptor agonist and amphetamine; dextroamphetamine use. If serotonin syndrome occurs, discontinue therapy. Concomitant use increases the risk for serotonin syndrome.
Alogliptin: (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking dipeptidyl peptidase-4 (DPP-4) inhibitors. Sympathomimetics, through stimulation of alpha- and beta-receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.
Alogliptin; metFORMIN: (Moderate) Monitor for loss of glycemic control when amphetamines are administered to patients taking antidiabetic agents. Sympathomimetic agents and adrenergic agonists tend to increase blood glucose concentrations when administered systemically. Sympathomimetic agents, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking dipeptidyl peptidase-4 (DPP-4) inhibitors. Sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients

taking medications for diabetes.
Alogliptin; Pioglitazone: (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking dipeptidyl peptidase-4 (DPP-4) inhibitors. Sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes. (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking thiazolidinediones. Sympathomimetics, through stimulation of alpha- and beta-receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.
Alpha-glucosidase Inhibitors: (Moderate) Sympathomimetic agents and adrenergic agonists tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when pseudoephedrine, phenylephrine, and other sympathomimetics are administered to patients taking antidiabetic agents. Epinephrine and other sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.
Aluminum Hydroxide: (Minor) Monitor for an increase in amphetamine-related adverse effects during concomitant antacid use. Increasing gastric or urine pH may increase amphetamine exposure and the risk for side effects in some patients. As antacids have rarely been observed to increase gastric or urinary pH above 6.5, antacid-related pH changes may be insufficient to warrant clinical concern in most patients.
Aluminum Hydroxide; Magnesium Carbonate: (Minor) Monitor for an increase in amphetamine-related adverse effects during concomitant antacid use. Increasing gastric or urine pH may increase amphetamine exposure and the risk for side effects in some patients. As antacids have rarely been observed to increase gastric or urinary pH above 6.5, antacid-related pH changes may be insufficient to warrant clinical concern in most patients.
Aluminum Hydroxide; Magnesium Hydroxide: (Minor) Monitor for an increase in

amphetamine-related adverse effects during concomitant antacid use. Increasing gastric or urine pH may increase amphetamine exposure and the risk for side effects in some patients. As antacids have rarely been observed to increase gastric or urinary pH above 6.5, antacid-related pH changes may be insufficient to warrant clinical concern in most patients.
Aluminum Hydroxide; Magnesium Hydroxide; Simethicone: (Minor) Monitor for an increase in amphetamine-related adverse effects during concomitant antacid use. Increasing gastric or urine pH may increase amphetamine exposure and the risk for side effects in some patients. As antacids have rarely been observed to increase gastric or urinary pH above 6.5, antacid-related pH changes may be insufficient to warrant clinical concern in most patients.
Aluminum Hydroxide; Magnesium Trisilicate: (Minor) Monitor for an increase in amphetamine-related adverse effects during concomitant antacid use. Increasing gastric or urine pH may increase amphetamine exposure and the risk for side effects in some patients. As antacids have rarely been observed to increase gastric or urinary pH above 6.5, antacid-related pH changes may be insufficient to warrant clinical concern in most patients.
Amantadine: (Moderate) Careful observation is required when amantadine is administered concurrently with central nervous system (CNS) stimulants. An increase in stimulant effects, such as nervousness, irritability, insomnia, tremor, seizures, or cardiac arrhythmias may occur.
Ambrisentan: (Minor) Sympathomimetics such as amphetamine or dextroamphetamine can antagonize the effects of vasodilators when administered concomitantly. Patients should be monitored for reduced efficacy of ambrisentan.
Amifampridine: (Major) Carefully consider the need for concomitant treatment with amphetamines and amifampridine, as coadministration may increase the risk of seizures. If coadministration occurs, closely monitor patients for seizure activity. Seizures have been observed in patients without a history of seizures taking amifampridine at recommended doses. Amphetamines may increase the risk of seizures.
aMILoride: (Minor) Amphetamines increase both systolic and diastolic blood pressure and may counteract the activity of some antihypertensive agents, like potassium-sparing diuretics. Close monitoring of blood pressure is advised.
aMILoride; hydroCHLOROthiazide, HCTZ: (Minor) Amphetamines increase both systolic and diastolic blood pressure and may counteract the activity of some antihypertensive agents, like potassium-sparing diuretics. Close monitoring of blood pressure is advised. (Minor) Amphetamines may counteract the activity of some antihypertensive agents, such as thiazide diuretics. Close monitoring of blood pressure is advised. Thiazide diuretics may also increase and prolong the actions of amphetamines by increasing the urinary pH.

Amitriptyline: (Moderate) Monitor blood pressure, heart rate, and for signs and symptoms of serotonin syndrome, particularly during treatment initiation and dosage increase, during concomitant amphetamine and tricyclic antidepressant use. Adjust doses or use alternative therapy based on clinical response. If serotonin syndrome occurs, discontinue therapy. Concomitant use increases the risk for potentiation of cardiovascular effects and serotonin syndrome. Amphetamines may enhance the activity of tricyclic antidepressants causing significant and sustained increases in amphetamine concentrations in the brain.
amLODIPine: (Minor) Amphetamines increase both systolic and diastolic blood pressure and may counteract the activity of some antihypertensive agents, like calcium-channel blockers. Close monitoring of blood pressure is advised.
amLODIPine; Atorvastatin: (Minor) Amphetamines increase both systolic and diastolic blood pressure and may counteract the activity of some antihypertensive agents, like calcium-channel blockers. Close monitoring of blood pressure is advised.
amLODIPine; Benazepril: (Minor) Amphetamines increase both systolic and diastolic blood pressure and may counteract the activity of some antihypertensive agents, like angiotensin-converting enzyme inhibitors (ACE inhibitors). Close monitoring of blood pressure is advised. (Minor) Amphetamines increase both systolic and diastolic blood pressure and may counteract the activity of some antihypertensive agents, like calcium-channel blockers. Close monitoring of blood pressure is advised.
amLODIPine; Celecoxib: (Minor) Amphetamines increase both systolic and diastolic blood pressure and may counteract the activity of some antihypertensive agents, like calcium-channel blockers. Close monitoring of blood pressure is advised.
amLODIPine; Olmesartan: (Minor) Amphetamines increase both systolic and diastolic blood pressure and may counteract the activity of some antihypertensive agents, like calcium-channel blockers. Close monitoring of blood pressure is advised. (Minor) Amphetamines increase both systolic and diastolic blood pressure and may counteract the activity of some antihypertensive agents, such as angiotensin II receptor antagonists. Close monitoring of blood pressure is advised.
amLODIPine; Valsartan: (Minor) Amphetamines increase both systolic and diastolic blood pressure and may counteract the activity of some antihypertensive agents, like calcium-channel blockers. Close monitoring of blood pressure is advised. (Minor) Amphetamines increase both systolic and diastolic blood pressure and may counteract the activity of some antihypertensive agents, such as angiotensin II receptor antagonists. Close monitoring of blood pressure is advised.
amLODIPine; Valsartan; hydroCHLOROthiazide, HCTZ: (Minor) Amphetamines increase both systolic and diastolic blood pressure and may counteract the activity of some antihypertensive agents, like calcium-channel blockers. Close monitoring of blood pressure is advised. (Minor) Amphetamines increase both systolic and diastolic blood pressure and may counteract the activity of some antihypertensive agents, such as

angiotensin II receptor antagonists. Close monitoring of blood pressure is advised.
(Minor) Amphetamines may counteract the activity of some antihypertensive agents, such as thiazide diuretics. Close monitoring of blood pressure is advised. Thiazide diuretics may also increase and prolong the actions of amphetamines by increasing the urinary pH.
Amoxapine: (Major) Concomitant use of amoxapine with sympathomimetics should be avoided whenever possible; use with caution when concurrent use cannot be avoided. One drug information reference suggests that cyclic antidepressants potentiate the pharmacologic effects of indirect-acting sympathomimetics, such as amphetamine, however, the data are not consistent.
Amoxicillin; Clarithromycin; Omeprazole: (Moderate) Use amphetamine; dextroamphetamine and proton pump inhibitors concomitantly with caution. Gastrointestinal alkalinizing agents may increase exposure to amphetamine; dextroamphetamine and exacerbate its actions.
Angiotensin II receptor antagonists: (Minor) Amphetamines increase both systolic and diastolic blood pressure and may counteract the activity of some antihypertensive agents, such as angiotensin II receptor antagonists. Close monitoring of blood pressure is advised.
Angiotensin-converting enzyme inhibitors: (Minor) Amphetamines increase both systolic and diastolic blood pressure and may counteract the activity of some antihypertensive agents, like angiotensin-converting enzyme inhibitors (ACE inhibitors). Close monitoring of blood pressure is advised.
Antacids: (Minor) Monitor for an increase in amphetamine-related adverse effects during concomitant antacid use. Increasing gastric or urine pH may increase amphetamine exposure and the risk for side effects in some patients. As antacids have rarely been observed to increase gastric or urinary pH above 6.5, antacid-related pH changes may be insufficient to warrant clinical concern in most patients.
Arformoterol: (Moderate) Caution and close observation should be used when arformoterol is used concurrently with other adrenergic sympathomimetics, administered by any route, to avoid potential for increased cardiovascular effects.
Armodafinil: (Moderate) The use of armodafinil with other psychostimulants, including amphetamines, (e.g., dextroamphetamine, lisdexamfetamine, amphetamine) has not been studied. In a single-dose study of dextroamphetamine combined with modafinil, a racemic compound containing armodafinil, no pharmacokinetic interactions occurred but a slight increase in stimulant-associated side effects was noted. Patients receiving combination therapy of armodafinil with other psychostimulants should be closely observed for signs of nervousness, irritability, insomnia, arrhythmias, or other stimulant-related side effects.
Articaine; EPINEPHrine: (Moderate) Monitor blood pressure and heart rate during concomitant amphetamine and epinephrine use. Amphetamines may potentiate the

pressor effects of epinephrine.
Ascorbic Acid, Vitamin C: (Moderate) Concurrent use of amphetamines and gastrointestinal acidifying agents, such as ascorbic acid, vitamin C, should be used with caution. Vitamin C lowers the absorption of amphetamines, resulting in reduced efficacy. It may be advisable to separate times of administration. In addition, ascorbic acid acts as a urinary acidifier, which reduces the renal tubular reabsorption of amphetamines, accelerating amphetamine clearance and reducing the duration of effect. If combined use is necessary, the amphetamine dose should be adjusted according to clinical response as needed.
Aspirin, ASA; Butalbital; Caffeine: (Moderate) Avoid excessive caffeine intake during use of the amphetamine salts. Caffeine is a CNS-stimulant and such actions are expected to be additive when coadministered with other CNS stimulants or psychostimulants. Excessive caffeine ingestion (via medicines, foods like chocolate, dietary supplements, or beverages including coffee, green tea, other teas, colas) may contribute to side effects like nervousness, irritability, nausea, insomnia, or tremor. Patients should avoid medications and dietary supplements which contain high amounts of caffeine.
Aspirin, ASA; Caffeine: (Moderate) Avoid excessive caffeine intake during use of the amphetamine salts. Caffeine is a CNS-stimulant and such actions are expected to be additive when coadministered with other CNS stimulants or psychostimulants. Excessive caffeine ingestion (via medicines, foods like chocolate, dietary supplements, or beverages including coffee, green tea, other teas, colas) may contribute to side effects like nervousness, irritability, nausea, insomnia, or tremor. Patients should avoid medications and dietary supplements which contain high amounts of caffeine.
Aspirin, ASA; Caffeine; Orphenadrine: (Moderate) Avoid excessive caffeine intake during use of the amphetamine salts. Caffeine is a CNS-stimulant and such actions are expected to be additive when coadministered with other CNS stimulants or psychostimulants. Excessive caffeine ingestion (via medicines, foods like chocolate, dietary supplements, or beverages including coffee, green tea, other teas, colas) may contribute to side effects like nervousness, irritability, nausea, insomnia, or tremor. Patients should avoid medications and dietary supplements which contain high amounts of caffeine.
Aspirin, ASA; Carisoprodol; Codeine: (Moderate) If concomitant use of codeine and amphetamines is warranted, monitor patients for the emergence of serotonin syndrome. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs. The concomitant use of opioids with other drugs that affect the serotonergic neurotransmitter system has resulted in serotonin syndrome.
Aspirin, ASA; Citric Acid; Sodium Bicarbonate: (Moderate) Monitor for an increase in the incidence and severity of amphetamine-related adverse effects during concomitant use of urinary alkalinizing agents. Increasing urine pH may increase amphetamine exposure by reducing urinary excretion of amphetamine. A urine pH more than 7.5 has been

observed to increase the half-life of amphetamine from 8 to 10.5 hours to 16 to 31 hours when compared to a pH less than 6. Additionally, a urine pH more than 8 has been observed to reduce the amount of amphetamine excreted in the urine over 16 hours to less than 3% of the original dose; a 5-fold reduction compared to controls.
Aspirin, ASA; Omeprazole: (Moderate) Use amphetamine; dextroamphetamine and proton pump inhibitors concomitantly with caution. Gastrointestinal alkalinizing agents may increase exposure to amphetamine; dextroamphetamine and exacerbate its actions.
Aspirin, ASA; oxyCODONE: (Moderate) If concomitant use of oxycodone and amphetamines is warranted, monitor patients for the emergence of serotonin syndrome. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs. The concomitant use of opioids with other drugs that affect the serotonergic neurotransmitter system has resulted in serotonin syndrome.
Atenolol: (Moderate) Monitor hemodynamic parameters and for loss of efficacy during concomitant sympathomimetic agent and beta-blocker use; dosage adjustments may be necessary. Concomitant use may antagonize the cardiovascular effects of either drug.
Atenolol; Chlorthalidone: (Moderate) Monitor hemodynamic parameters and for loss of efficacy during concomitant sympathomimetic agent and beta-blocker use; dosage adjustments may be necessary. Concomitant use may antagonize the cardiovascular effects of either drug. (Minor) Amphetamines may counteract the activity of some antihypertensive agents, such as thiazide diuretics. Close monitoring of blood pressure is advised. Thiazide diuretics may also increase and prolong the actions of amphetamines by increasing the urinary pH.
Atomoxetine: (Moderate) Monitor blood pressure during concomitant amphetamine; dextroamphetamine and atomoxetine use. Because of possible effects on blood pressure, atomoxetine should be used cautiously with other drugs that affect blood pressure, such as amphetamine; dextroamphetamine.
Azilsartan: (Minor) Amphetamines increase both systolic and diastolic blood pressure and may counteract the activity of some antihypertensive agents, such as angiotensin II receptor antagonists. Close monitoring of blood pressure is advised.
Azilsartan; Chlorthalidone: (Minor) Amphetamines increase both systolic and diastolic blood pressure and may counteract the activity of some antihypertensive agents, such as angiotensin II receptor antagonists. Close monitoring of blood pressure is advised. (Minor) Amphetamines may counteract the activity of some antihypertensive agents, such as thiazide diuretics. Close monitoring of blood pressure is advised. Thiazide diuretics may also increase and prolong the actions of amphetamines by increasing the urinary pH.
Benazepril: (Minor) Amphetamines increase both systolic and diastolic blood pressure and may counteract the activity of some antihypertensive agents, like angiotensin-converting enzyme inhibitors (ACE inhibitors). Close monitoring of blood pressure is

advised.
Benazepril; hydroCHLOROthiazide, HCTZ: (Minor) Amphetamines increase both systolic and diastolic blood pressure and may counteract the activity of some antihypertensive agents, like angiotensin-converting enzyme inhibitors (ACE inhibitors). Close monitoring of blood pressure is advised. (Minor) Amphetamines may counteract the activity of some antihypertensive agents, such as thiazide diuretics. Close monitoring of blood pressure is advised. Thiazide diuretics may also increase and prolong the actions of amphetamines by increasing the urinary pH.
Benzoic Acid; Hyoscyamine; Methenamine; Methylene Blue; Phenyl Salicylate: (Contraindicated) Amphetamines should not be administered during or within 14 days after the use of methylene blue. Methylene blue is a potent, reversible monoamine oxidase inhibitor (MAOI) which can prolong and intensify the cardiac stimulation and vasopressor effects of amphetamines, potentially resulting in hypertensive crisis. Methylene blue also has the potential to interact with serotonergic agents, such as amphetamines, which may increase the risk for serotonin syndrome. Serotonin syndrome is characterized by 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, gastrointestinal symptoms (e.g., nausea, vomiting, diarrhea), and in rare instances, death. Cases of serotonin syndrome have been reported, primarily following administration of standard infusions of methylene blue (1 to 8 mg/kg) as a visualizing agent in parathyroid surgery, in patients receiving selective serotonin reuptake inhibitors, serotonin/norepinephrine reuptake inhibitors, or clomipramine. It is not known if patients receiving other serotonergic psychiatric agents, such as amphetamines, with intravenous methylene blue are at a comparable risk or if methylene blue administered by other routes (e.g., orally, local injection) or in doses less than 1 mg/kg IV can produce a similar outcome. Published interaction reports between intravenously administered methylene blue and serotonergic psychiatric agents have documented symptoms including lethargy, confusion, delirium, agitation, aggression, obtundation, myoclonus, expressive aphasia, hypertonia, pyrexia, elevated blood pressure, seizures, and/or coma. (Major) Urinary acidifying agents, such as ammonium chloride, phosphorus salts, and methenamine salts (e.g., methenamine; sodium acid phosphate), reduce the tubular reabsorption of amphetamines. As a result, amphetamine clearance is accelerated and the duration of effect is reduced. Combination therapy should be avoided if possible.
Beta-blockers: (Moderate) Monitor hemodynamic parameters and for loss of efficacy during concomitant sympathomimetic agent and beta-blocker use; dosage adjustments may be necessary. Concomitant use may antagonize the cardiovascular effects of either drug.
Betaxolol: (Moderate) Monitor hemodynamic parameters and for loss of efficacy during

concomitant sympathomimetic agent and beta-blocker use; dosage adjustments may be necessary. Concomitant use may antagonize the cardiovascular effects of either drug.
Bethanechol: (Moderate) Bethanechol offsets the effects of sympathomimetics at sites where sympathomimetic and cholinergic receptors have opposite effects.
Bexagliflozin: (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking SGLT2 inhibitors. Sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.
Bisoprolol: (Moderate) Monitor hemodynamic parameters and for loss of efficacy during concomitant sympathomimetic agent and beta-blocker use; dosage adjustments may be necessary. Concomitant use may antagonize the cardiovascular effects of either drug.
Bisoprolol; hydroCHLOROthiazide, HCTZ: (Moderate) Monitor hemodynamic parameters and for loss of efficacy during concomitant sympathomimetic agent and beta-blocker use; dosage adjustments may be necessary. Concomitant use may antagonize the cardiovascular effects of either drug. (Minor) Amphetamines may counteract the activity of some antihypertensive agents, such as thiazide diuretics. Close monitoring of blood pressure is advised. Thiazide diuretics may also increase and prolong the actions of amphetamines by increasing the urinary pH.
Bretylium: (Moderate) Monitor blood pressure and heart rate closely when sympathomimetics are administered with bretylium. The pressor and arrhythmogenic effects of catecholamines are enhanced by bretylium.
Brimonidine; Timolol: (Moderate) Monitor hemodynamic parameters and for loss of efficacy during concomitant sympathomimetic agent and beta-blocker use; dosage adjustments may be necessary. Concomitant use may antagonize the cardiovascular effects of either drug.
Bromocriptine: (Moderate) Concurrent use of bromocriptine and some sympathomimetics such as amphetamines should be approached with caution. One case report documented worsening headache, hypertension, premature ventricular complexes, and ventricular tachycardia in a post-partum patient receiving bromocriptine for lactation suppression who was subsequently prescribed an isometheptene-containing medication for a headache. A second case involved a post-partum patient receiving bromocriptine who was later prescribed a phenylpropanolamine-expectorant combination and subsequently developed hypertension, tachycardia, seizures, and cerebral vasospasm.
Brompheniramine: (Moderate) Amphetamines may pharmacodynamically counteract

the sedative properties of some antihistamines, such as the sedating H1-blockers (i.e., diphenhydramine). This effect may be clinically important if a patient is receiving an antihistamine agent for treatment of insomnia. Alternatively, if a patient is receiving an amphetamine for treatment of narcolepsy, the combination with a sedating antihistamine may reverse the action of the amphetamine.
Brompheniramine; Dextromethorphan; Phenylephrine: (Moderate) Amphetamines may pharmacodynamically counteract the sedative properties of some antihistamines, such as the sedating H1-blockers (i.e., diphenhydramine). This effect may be clinically important if a patient is receiving an antihistamine agent for treatment of insomnia. Alternatively, if a patient is receiving an amphetamine for treatment of narcolepsy, the combination with a sedating antihistamine may reverse the action of the amphetamine.
Brompheniramine; Phenylephrine: (Moderate) Amphetamines may pharmacodynamically counteract the sedative properties of some antihistamines, such as the sedating H1-blockers (i.e., diphenhydramine). This effect may be clinically important if a patient is receiving an antihistamine agent for treatment of insomnia. Alternatively, if a patient is receiving an amphetamine for treatment of narcolepsy, the combination with a sedating antihistamine may reverse the action of the amphetamine.
Brompheniramine; Pseudoephedrine: (Moderate) Amphetamines may pharmacodynamically counteract the sedative properties of some antihistamines, such as the sedating H1-blockers (i.e., diphenhydramine). This effect may be clinically important if a patient is receiving an antihistamine agent for treatment of insomnia. Alternatively, if a patient is receiving an amphetamine for treatment of narcolepsy, the combination with a sedating antihistamine may reverse the action of the amphetamine.
Brompheniramine; Pseudoephedrine; Dextromethorphan: (Moderate) Amphetamines may pharmacodynamically counteract the sedative properties of some antihistamines, such as the sedating H1-blockers (i.e., diphenhydramine). This effect may be clinically important if a patient is receiving an antihistamine agent for treatment of insomnia. Alternatively, if a patient is receiving an amphetamine for treatment of narcolepsy, the combination with a sedating antihistamine may reverse the action of the amphetamine.
Budesonide; Formoterol: (Moderate) Monitor blood pressure and heart rate during concomitant amphetamine; dextroamphetamine and formoterol use. Concomitant use may potentiate sympathetic effects.
Budesonide; Glycopyrrolate; Formoterol: (Moderate) Monitor blood pressure and heart rate during concomitant amphetamine; dextroamphetamine and formoterol use. Concomitant use may potentiate sympathetic effects.
Bumetanide: (Minor) Amphetamine and Dextroamphetamine may increase both systolic and diastolic blood pressure and may counteract the activity of some antihypertensive agents, such as loop diuretics. Close monitoring of blood pressure is advised.
BUPivacaine; EPINEPHrine: (Moderate) Monitor blood pressure and heart rate during concomitant amphetamine and epinephrine use. Amphetamines may potentiate the

pressor effects of epinephrine.
Buprenorphine: (Moderate) If concomitant use of buprenorphine and amphetamines is warranted, monitor patients for the emergence of serotonin syndrome. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs. The concomitant use of opioids with other drugs that affect the serotonergic neurotransmitter system has resulted in serotonin syndrome.
Buprenorphine; Naloxone: (Moderate) If concomitant use of buprenorphine and amphetamines is warranted, monitor patients for the emergence of serotonin syndrome. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs. The concomitant use of opioids with other drugs that affect the serotonergic neurotransmitter system has resulted in serotonin syndrome.
buPROPion: (Moderate) Use extreme caution when coadministering bupropion with other drugs that lower the seizure threshold, such as stimulants including amphetamine; dextroamphetamine. Use low initial doses of bupropion and increase the dose gradually.
buPROPion; Naltrexone: (Moderate) Use extreme caution when coadministering bupropion with other drugs that lower the seizure threshold, such as stimulants including amphetamine; dextroamphetamine. Use low initial doses of bupropion and increase the dose gradually.
busPIRone: (Moderate) Coadministration of buspirone with amphetamines may increase the risk of serotonin syndrome. At high doses, amphetamines can increase serotonin release and act as serotonin agonists. Buspirone has some serotonergic properties. Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome, particularly during treatment initiation and dose increases. If serotonin syndrome occurs, all serotonergic drugs should be discontinued and appropriate medical treatment should be initiated.
Butalbital; Acetaminophen; Caffeine: (Moderate) Avoid excessive caffeine intake during use of the amphetamine salts. Caffeine is a CNS-stimulant and such actions are expected to be additive when coadministered with other CNS stimulants or psychostimulants. Excessive caffeine ingestion (via medicines, foods like chocolate, dietary supplements, or beverages including coffee, green tea, other teas, colas) may contribute to side effects like nervousness, irritability, nausea, insomnia, or tremor. Patients should avoid medications and dietary supplements which contain high amounts of caffeine.
Butalbital; Acetaminophen; Caffeine; Codeine: (Moderate) Avoid excessive caffeine intake during use of the amphetamine salts. Caffeine is a CNS-stimulant and such actions are expected to be additive when coadministered with other CNS stimulants or psychostimulants. Excessive caffeine ingestion (via medicines, foods like chocolate, dietary supplements, or beverages including coffee, green tea, other teas, colas) may contribute to side effects like nervousness, irritability, nausea, insomnia, or tremor.

Patients should avoid medications and dietary supplements which contain high amounts of caffeine. (Moderate) If concomitant use of codeine and amphetamines is warranted, monitor patients for the emergence of serotonin syndrome. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs. The concomitant use of opioids with other drugs that affect the serotonergic neurotransmitter system has resulted in serotonin syndrome.
Butalbital; Aspirin; Caffeine; Codeine: (Moderate) Avoid excessive caffeine intake during use of the amphetamine salts. Caffeine is a CNS-stimulant and such actions are expected to be additive when coadministered with other CNS stimulants or psychostimulants. Excessive caffeine ingestion (via medicines, foods like chocolate, dietary supplements, or beverages including coffee, green tea, other teas, colas) may contribute to side effects like nervousness, irritability, nausea, insomnia, or tremor. Patients should avoid medications and dietary supplements which contain high amounts of caffeine. (Moderate) If concomitant use of codeine and amphetamines is warranted, monitor patients for the emergence of serotonin syndrome. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs. The concomitant use of opioids with other drugs that affect the serotonergic neurotransmitter system has resulted in serotonin syndrome.
Caffeine: (Moderate) Avoid excessive caffeine intake during use of the amphetamine salts. Caffeine is a CNS-stimulant and such actions are expected to be additive when coadministered with other CNS stimulants or psychostimulants. Excessive caffeine ingestion (via medicines, foods like chocolate, dietary supplements, or beverages including coffee, green tea, other teas, colas) may contribute to side effects like nervousness, irritability, nausea, insomnia, or tremor. Patients should avoid medications and dietary supplements which contain high amounts of caffeine. (Moderate) CNS-stimulating actions of caffeine can be additive with other CNS stimulants. Patients may need to reduce, limit, or avoid caffeine intake. Excessive caffeine ingestion (via medicines, supplements or beverages including coffee, green tea, other teas, guarana, colas) may contribute to side effects like nervousness, irritability, insomnia, or tremor.
Caffeine; Sodium Benzoate: (Moderate) Avoid excessive caffeine intake during use of the amphetamine salts. Caffeine is a CNS-stimulant and such actions are expected to be additive when coadministered with other CNS stimulants or psychostimulants. Excessive caffeine ingestion (via medicines, foods like chocolate, dietary supplements, or beverages including coffee, green tea, other teas, colas) may contribute to side effects like nervousness, irritability, nausea, insomnia, or tremor. Patients should avoid medications and dietary supplements which contain high amounts of caffeine.
Calcium Carbonate: (Minor) Monitor for an increase in amphetamine-related adverse effects during concomitant antacid use. Increasing gastric or urine pH may increase amphetamine exposure and the risk for side effects in some patients. As antacids have rarely been observed to increase gastric or urinary pH above 6.5, antacid-related pH

changes may be insufficient to warrant clinical concern in most patients.
Calcium Carbonate; Famotidine; Magnesium Hydroxide: (Moderate) Use amphetamine; dextroamphetamine and H2-blockers concomitantly with caution. Gastrointestinal alkalinizing agents may increase exposure to amphetamine; dextroamphetamine and exacerbate its actions. (Minor) Monitor for an increase in amphetamine-related adverse effects during concomitant antacid use. Increasing gastric or urine pH may increase amphetamine exposure and the risk for side effects in some patients. As antacids have rarely been observed to increase gastric or urinary pH above 6.5, antacid-related pH changes may be insufficient to warrant clinical concern in most patients.
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Calcium Carbonate; Magnesium Hydroxide; Simethicone: (Minor) Monitor for an increase in amphetamine-related adverse effects during concomitant antacid use. Increasing gastric or urine pH may increase amphetamine exposure and the risk for side effects in some patients. As antacids have rarely been observed to increase gastric or urinary pH above 6.5, antacid-related pH changes may be insufficient to warrant clinical concern in most patients.
Calcium Carbonate; Simethicone: (Minor) Monitor for an increase in amphetamine-related adverse effects during concomitant antacid use. Increasing gastric or urine pH may increase amphetamine exposure and the risk for side effects in some patients. As antacids have rarely been observed to increase gastric or urinary pH above 6.5, antacid-related pH changes may be insufficient to warrant clinical concern in most patients.
Calcium, Magnesium, Potassium, Sodium Oxybates: (Moderate) Sodium oxybate has the potential to induce seizures; it has been speculated that this effect may be mediated through the action of sodium oxybate at GABA receptors. Although convulsant effects occur primarily at high dosages, sodium oxybate should be used cautiously with psychostimulants that are known to lower seizure threshold such as the amphetamines. Note that CNS stimulants, including the amphetamines, are frequently used in the treatment of narcolepsy, and clinical trials involving the use of psychostimulants with sodium oxybate have not found the combinations to be unsafe. Pharmacodynamic interactions cannot be ruled out, however.
Calcium; Vitamin D: (Minor) Monitor for an increase in amphetamine-related adverse effects during concomitant antacid use. Increasing gastric or urine pH may increase amphetamine exposure and the risk for side effects in some patients. As antacids have rarely been observed to increase gastric or urinary pH above 6.5, antacid-related pH changes may be insufficient to warrant clinical concern in most patients.

Calcium-channel blockers: (Minor) Amphetamines increase both systolic and diastolic blood pressure and may counteract the activity of some antihypertensive agents, like calcium-channel blockers. Close monitoring of blood pressure is advised.
Canagliflozin: (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking SGLT2 inhibitors. Sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.
Canagliflozin; metFORMIN: (Moderate) Monitor for loss of glycemic control when amphetamines are administered to patients taking antidiabetic agents. Sympathomimetic agents and adrenergic agonists tend to increase blood glucose concentrations when administered systemically. Sympathomimetic agents, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking SGLT2 inhibitors. Sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.
Candesartan: (Minor) Amphetamines increase both systolic and diastolic blood pressure and may counteract the activity of some antihypertensive agents, such as angiotensin II receptor antagonists. Close monitoring of blood pressure is advised.
Candesartan; hydroCHLOROthiazide, HCTZ: (Minor) Amphetamines increase both systolic and diastolic blood pressure and may counteract the activity of some antihypertensive agents, such as angiotensin II receptor antagonists. Close monitoring of blood pressure is advised. (Minor) Amphetamines may counteract the activity of some antihypertensive agents, such as thiazide diuretics. Close monitoring of blood pressure is advised. Thiazide diuretics may also increase and prolong the actions of amphetamines by increasing the urinary pH.
Captopril: (Minor) Amphetamines increase both systolic and diastolic blood pressure and may counteract the activity of some antihypertensive agents, like angiotensin-converting enzyme inhibitors (ACE inhibitors). Close monitoring of blood pressure is

advised.
Captopril; hydroCHLOROthiazide, HCTZ: (Minor) Amphetamines increase both systolic and diastolic blood pressure and may counteract the activity of some antihypertensive agents, like angiotensin-converting enzyme inhibitors (ACE inhibitors). Close monitoring of blood pressure is advised. (Minor) Amphetamines may counteract the activity of some antihypertensive agents, such as thiazide diuretics. Close monitoring of blood pressure is advised. Thiazide diuretics may also increase and prolong the actions of amphetamines by increasing the urinary pH.
Carbinoxamine: (Moderate) Amphetamines may pharmacodynamically counteract the sedative properties of some antihistamines, such as the sedating H1-blockers (i.e., diphenhydramine). This effect may be clinically important if a patient is receiving an antihistamine agent for treatment of insomnia. Alternatively, if a patient is receiving an amphetamine for treatment of narcolepsy, the combination with a sedating antihistamine may reverse the action of the amphetamine.
Carteolol: (Moderate) Monitor hemodynamic parameters and for loss of efficacy during concomitant sympathomimetic agent and beta-blocker use; dosage adjustments may be necessary. Concomitant use may antagonize the cardiovascular effects of either drug.
Carvedilol: (Moderate) Monitor hemodynamic parameters and for loss of efficacy during concomitant sympathomimetic agent and beta-blocker use; dosage adjustments may be necessary. Concomitant use may antagonize the cardiovascular effects of either drug.
Celecoxib; Tramadol: (Major) Because of the potential risk and severity of serotonin syndrome, caution should be observed when administering amphetamines with other drugs that have serotonergic properties such as tramadol. Serotonin syndrome is characterized by the rapid development of hyperthermia, hypertension, myoclonus, rigidity, autonomic instability, mental status changes (e.g., delirium or coma), and in rare cases, death. Further study is needed to fully elucidate the severity and frequency of adverse effects that may occur from concomitant administration of amphetamines and tramadol. Patients receiving tramadol and an amphetamine should be monitored for the emergence of serotonin syndrome, particularly during treatment initiation and during dosage increases. The amphetamine and tramadol should be discontinued if serotonin syndrome occurs and supportive symptomatic treatment should be initiated. In addition, the risk of seizures from the use of tramadol may be increased with concomitant use of CNS stimulants that may induce seizures, including the amphetamines. Extreme caution and close clinical monitoring is recommended if these agents must be used together.
Chlophedianol; Dexbrompheniramine: (Moderate) Amphetamines may pharmacodynamically counteract the sedative properties of some antihistamines, such as the sedating H1-blockers (i.e., diphenhydramine). This effect may be clinically important if a patient is receiving an antihistamine agent for treatment of insomnia. Alternatively, if a patient is receiving an amphetamine for treatment of narcolepsy, the

combination with a sedating antihistamine may reverse the action of the amphetamine.
Chlophedianol; Dexchlorpheniramine; Pseudoephedrine: (Moderate) Amphetamines may pharmacodynamically counteract the sedative properties of some antihistamines, such as the sedating H1-blockers (i.e., diphenhydramine). This effect may be clinically important if a patient is receiving an antihistamine agent for treatment of insomnia. Alternatively, if a patient is receiving an amphetamine for treatment of narcolepsy, the combination with a sedating antihistamine may reverse the action of the amphetamine.
Chlorcyclizine: (Moderate) Amphetamines may pharmacodynamically counteract the sedative properties of some antihistamines, such as the sedating H1-blockers (i.e., diphenhydramine). This effect may be clinically important if a patient is receiving an antihistamine agent for treatment of insomnia. Alternatively, if a patient is receiving an amphetamine for treatment of narcolepsy, the combination with a sedating antihistamine may reverse the action of the amphetamine.
chlordiazePOXIDE; Amitriptyline: (Moderate) Monitor blood pressure, heart rate, and for signs and symptoms of serotonin syndrome, particularly during treatment initiation and dosage increase, during concomitant amphetamine and tricyclic antidepressant use. Adjust doses or use alternative therapy based on clinical response. If serotonin syndrome occurs, discontinue therapy. Concomitant use increases the risk for potentiation of cardiovascular effects and serotonin syndrome. Amphetamines may enhance the activity of tricyclic antidepressants causing significant and sustained increases in amphetamine concentrations in the brain.
Chlorothiazide: (Minor) Amphetamines may counteract the activity of some antihypertensive agents, such as thiazide diuretics. Close monitoring of blood pressure is advised. Thiazide diuretics may also increase and prolong the actions of amphetamines by increasing the urinary pH.
Chlorpheniramine: (Moderate) Amphetamines may pharmacodynamically counteract the sedative properties of some antihistamines, such as the sedating H1-blockers (i.e., diphenhydramine). This effect may be clinically important if a patient is receiving an antihistamine agent for treatment of insomnia. Alternatively, if a patient is receiving an amphetamine for treatment of narcolepsy, the combination with a sedating antihistamine may reverse the action of the amphetamine.
Chlorpheniramine; Codeine: (Moderate) Amphetamines may pharmacodynamically counteract the sedative properties of some antihistamines, such as the sedating H1-blockers (i.e., diphenhydramine). This effect may be clinically important if a patient is receiving an antihistamine agent for treatment of insomnia. Alternatively, if a patient is receiving an amphetamine for treatment of narcolepsy, the combination with a sedating antihistamine may reverse the action of the amphetamine. (Moderate) If concomitant use of codeine and amphetamines is warranted, monitor patients for the emergence of serotonin syndrome. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs. The concomitant use of opioids with other

drugs that affect the serotonergic neurotransmitter system has resulted in serotonin syndrome.
Chlorpheniramine; Dextromethorphan: (Moderate) Amphetamines may pharmacodynamically counteract the sedative properties of some antihistamines, such as the sedating H1-blockers (i.e., diphenhydramine). This effect may be clinically important if a patient is receiving an antihistamine agent for treatment of insomnia. Alternatively, if a patient is receiving an amphetamine for treatment of narcolepsy, the combination with a sedating antihistamine may reverse the action of the amphetamine.
Chlorpheniramine; Dextromethorphan; Phenylephrine: (Moderate) Amphetamines may pharmacodynamically counteract the sedative properties of some antihistamines, such as the sedating H1-blockers (i.e., diphenhydramine). This effect may be clinically important if a patient is receiving an antihistamine agent for treatment of insomnia. Alternatively, if a patient is receiving an amphetamine for treatment of narcolepsy, the combination with a sedating antihistamine may reverse the action of the amphetamine.
Chlorpheniramine; Dextromethorphan; Pseudoephedrine: (Moderate) Amphetamines may pharmacodynamically counteract the sedative properties of some antihistamines, such as the sedating H1-blockers (i.e., diphenhydramine). This effect may be clinically important if a patient is receiving an antihistamine agent for treatment of insomnia. Alternatively, if a patient is receiving an amphetamine for treatment of narcolepsy, the combination with a sedating antihistamine may reverse the action of the amphetamine.
Chlorpheniramine; HYDROcodone: (Moderate) Amphetamines may pharmacodynamically counteract the sedative properties of some antihistamines, such as the sedating H1-blockers (i.e., diphenhydramine). This effect may be clinically important if a patient is receiving an antihistamine agent for treatment of insomnia. Alternatively, if a patient is receiving an amphetamine for treatment of narcolepsy, the combination with a sedating antihistamine may reverse the action of the amphetamine. (Moderate) If concomitant use of hydrocodone and amphetamines is warranted, monitor patients for the emergence of serotonin syndrome. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs. The concomitant use of opioids with other drugs that affect the serotonergic neurotransmitter system has resulted in serotonin syndrome.
Chlorpheniramine; Ibuprofen; Pseudoephedrine: (Moderate) Amphetamines may pharmacodynamically counteract the sedative properties of some antihistamines, such as the sedating H1-blockers (i.e., diphenhydramine). This effect may be clinically important if a patient is receiving an antihistamine agent for treatment of insomnia. Alternatively, if a patient is receiving an amphetamine for treatment of narcolepsy, the combination with a sedating antihistamine may reverse the action of the amphetamine.
Chlorpheniramine; Phenylephrine: (Moderate) Amphetamines may pharmacodynamically counteract the sedative properties of some antihistamines, such as the sedating H1-blockers (i.e., diphenhydramine). This effect may be clinically

important if a patient is receiving an antihistamine agent for treatment of insomnia. Alternatively, if a patient is receiving an amphetamine for treatment of narcolepsy, the combination with a sedating antihistamine may reverse the action of the amphetamine.
Chlorpheniramine; Pseudoephedrine: (Moderate) Amphetamines may pharmacodynamically counteract the sedative properties of some antihistamines, such as the sedating H1-blockers (i.e., diphenhydramine). This effect may be clinically important if a patient is receiving an antihistamine agent for treatment of insomnia. Alternatively, if a patient is receiving an amphetamine for treatment of narcolepsy, the combination with a sedating antihistamine may reverse the action of the amphetamine.
Chlorthalidone: (Minor) Amphetamines may counteract the activity of some antihypertensive agents, such as thiazide diuretics. Close monitoring of blood pressure is advised. Thiazide diuretics may also increase and prolong the actions of amphetamines by increasing the urinary pH.
Cimetidine: (Moderate) Use amphetamine; dextroamphetamine and H2-blockers concomitantly with caution. Gastrointestinal alkalinizing agents may increase exposure to amphetamine; dextroamphetamine and exacerbate its actions.
Citalopram: (Moderate) Coadministration of selective serotonin reuptake inhibitors (SSRIs) like citalopram with amphetamines may increase the risk of serotonin syndrome. At high doses, amphetamines can increase serotonin release and act as serotonin agonists. Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome, particularly during treatment initiation and dose increases. If serotonin syndrome occurs, serotonergic drugs should be discontinued and appropriate medical treatment should be initiated.
Citric Acid; Potassium Citrate; Sodium Citrate: (Moderate) Monitor for an increase in the incidence and severity of amphetamine-related adverse effects during concomitant use of urinary alkalinizing agents. Increasing urine pH may increase amphetamine exposure by reducing urinary excretion of amphetamine. A urine pH more than 7.5 has been observed to increase the half-life of amphetamine from 8 to 10.5 hours to 16 to 31 hours when compared to a pH less than 6. Additionally, a urine pH more than 8 has been observed to reduce the amount of amphetamine excreted in the urine over 16 hours to less than 3% of the original dose; a 5-fold reduction compared to controls.
Clemastine: (Moderate) Amphetamines may pharmacodynamically counteract the sedative properties of some antihistamines, such as the sedating H1-blockers (i.e., diphenhydramine). This effect may be clinically important if a patient is receiving an antihistamine agent for treatment of insomnia. Alternatively, if a patient is receiving an amphetamine for treatment of narcolepsy, the combination with a sedating antihistamine may reverse the action of the amphetamine.
Clevidipine: (Minor) Amphetamines increase both systolic and diastolic blood pressure and may counteract the activity of some antihypertensive agents, like calcium-channel blockers. Close monitoring of blood pressure is advised.

clomiPRAMINE: (Moderate) Monitor blood pressure, heart rate, and for signs and symptoms of serotonin syndrome, particularly during treatment initiation and dosage increase, during concomitant amphetamine and tricyclic antidepressant use. Adjust doses or use alternative therapy based on clinical response. If serotonin syndrome occurs, discontinue therapy. Concomitant use increases the risk for potentiation of cardiovascular effects and serotonin syndrome. Amphetamines may enhance the activity of tricyclic antidepressants causing significant and sustained increases in amphetamine concentrations in the brain.
cloNIDine: (Minor) Close monitoring of blood pressure or the selection of alternative therapeutic agents may be needed in patients receiving clonidine and amphetamines. Amphetamines increase both systolic and diastolic blood pressure and may counteract the activity of some antihypertensive agents.
Cocaine: (Major) Avoid concomitant use of additional vasoconstrictor agents with cocaine. If unavoidable, prolonged vital sign and ECG monitoring may be required. Myocardial ischemia, myocardial infarction, and ventricular arrhythmias have been reported after concomitant administration of topical intranasal cocaine and vasoconstrictor agents during nasal and sinus surgery. The risk for nervousness, irritability, convulsions, and other cardiac arrhythmias may increase during coadministration.
Codeine: (Moderate) If concomitant use of codeine and amphetamines is warranted, monitor patients for the emergence of serotonin syndrome. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs. The concomitant use of opioids with other drugs that affect the serotonergic neurotransmitter system has resulted in serotonin syndrome.
Codeine; Dexbrompheniramine: (Moderate) Amphetamines may pharmacodynamically counteract the sedative properties of some antihistamines, such as the sedating H1-blockers (i.e., diphenhydramine). This effect may be clinically important if a patient is receiving an antihistamine agent for treatment of insomnia. Alternatively, if a patient is receiving an amphetamine for treatment of narcolepsy, the combination with a sedating antihistamine may reverse the action of the amphetamine. (Moderate) If concomitant use of codeine and amphetamines is warranted, monitor patients for the emergence of serotonin syndrome. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs. The concomitant use of opioids with other drugs that affect the serotonergic neurotransmitter system has resulted in serotonin syndrome.
Codeine; guaiFENesin: (Moderate) If concomitant use of codeine and amphetamines is warranted, monitor patients for the emergence of serotonin syndrome. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs. The concomitant use of opioids with other drugs that affect the serotonergic neurotransmitter system has resulted in serotonin syndrome.

Codeine; guaiFENesin; Pseudoephedrine: (Moderate) If concomitant use of codeine and amphetamines is warranted, monitor patients for the emergence of serotonin syndrome. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs. The concomitant use of opioids with other drugs that affect the serotonergic neurotransmitter system has resulted in serotonin syndrome.
Codeine; Phenylephrine; Promethazine: (Moderate) If concomitant use of codeine and amphetamines is warranted, monitor patients for the emergence of serotonin syndrome. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs. The concomitant use of opioids with other drugs that affect the serotonergic neurotransmitter system has resulted in serotonin syndrome.
Codeine; Promethazine: (Moderate) If concomitant use of codeine and amphetamines is warranted, monitor patients for the emergence of serotonin syndrome. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs. The concomitant use of opioids with other drugs that affect the serotonergic neurotransmitter system has resulted in serotonin syndrome.
Cyproheptadine: (Moderate) Amphetamines may pharmacodynamically counteract the sedative properties of some antihistamines, such as the sedating H1-blockers (i.e., diphenhydramine). This effect may be clinically important if a patient is receiving an antihistamine agent for treatment of insomnia. Alternatively, if a patient is receiving an amphetamine for treatment of narcolepsy, the combination with a sedating antihistamine may reverse the action of the amphetamine.
Dacomitinib: (Moderate) Warn patients that the risk of amphetamine toxicity, including serotonin syndrome, may be increased during concurrent use with dacomitinib. Concurrent use of dacomitinib, a strong CYP2D6 inhibitor, may increase exposure to the amphetamine increasing the risk for serotonin syndrome. If serotonin syndrome occurs, both the amphetamine and dacomitinib should be discontinued and appropriate medical treatment should be implemented.
Dapagliflozin: (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking SGLT2 inhibitors. Sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.
Dapagliflozin; metFORMIN: (Moderate) Monitor for loss of glycemic control when amphetamines are administered to patients taking antidiabetic agents. Sympathomimetic agents and adrenergic agonists tend to increase blood glucose concentrations when administered systemically. Sympathomimetic agents, through

stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking SGLT2 inhibitors. Sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.
Dapagliflozin; sAXagliptin: (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking dipeptidyl peptidase-4 (DPP-4) inhibitors. Sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes. (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking SGLT2 inhibitors. Sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.
Desipramine: (Moderate) Monitor blood pressure, heart rate, and for signs and symptoms of serotonin syndrome, particularly during treatment initiation and dosage increase, during concomitant amphetamine and tricyclic antidepressant use. Adjust doses or use alternative therapy based on clinical response. If serotonin syndrome occurs, discontinue therapy. Concomitant use increases the risk for potentiation of cardiovascular effects and serotonin syndrome. Amphetamines may enhance the activity of tricyclic antidepressants causing significant and sustained increases in amphetamine concentrations in the brain.
Desvenlafaxine: (Moderate) Coadministration of amphetamines with serotonin norepinephrine reuptake inhibitors (SNRIs) may increase the risk of serotonin syndrome. At high doses, amphetamines can increase serotonin release and act as serotonin agonists. Inform patients taking this combination of the possible increased

risk and monitor for the emergence of serotonin syndrome, particularly during treatment initiation and dose increases. If serotonin syndrome occurs, serotonergic drugs should be discontinued and appropriate medical treatment should be initiated.
Dexbrompheniramine: (Moderate) Amphetamines may pharmacodynamically counteract the sedative properties of some antihistamines, such as the sedating H1-blockers (i.e., diphenhydramine). This effect may be clinically important if a patient is receiving an antihistamine agent for treatment of insomnia. Alternatively, if a patient is receiving an amphetamine for treatment of narcolepsy, the combination with a sedating antihistamine may reverse the action of the amphetamine.
Dexbrompheniramine; Dextromethorphan; Phenylephrine: (Moderate) Amphetamines may pharmacodynamically counteract the sedative properties of some antihistamines, such as the sedating H1-blockers (i.e., diphenhydramine). This effect may be clinically important if a patient is receiving an antihistamine agent for treatment of insomnia. Alternatively, if a patient is receiving an amphetamine for treatment of narcolepsy, the combination with a sedating antihistamine may reverse the action of the amphetamine.
Dexbrompheniramine; Pseudoephedrine: (Moderate) Amphetamines may pharmacodynamically counteract the sedative properties of some antihistamines, such as the sedating H1-blockers (i.e., diphenhydramine). This effect may be clinically important if a patient is receiving an antihistamine agent for treatment of insomnia. Alternatively, if a patient is receiving an amphetamine for treatment of narcolepsy, the combination with a sedating antihistamine may reverse the action of the amphetamine.
Dexchlorpheniramine: (Moderate) Amphetamines may pharmacodynamically counteract the sedative properties of some antihistamines, such as the sedating H1-blockers (i.e., diphenhydramine). This effect may be clinically important if a patient is receiving an antihistamine agent for treatment of insomnia. Alternatively, if a patient is receiving an amphetamine for treatment of narcolepsy, the combination with a sedating antihistamine may reverse the action of the amphetamine.
Dexchlorpheniramine; Dextromethorphan; Pseudoephedrine: (Moderate) Amphetamines may pharmacodynamically counteract the sedative properties of some antihistamines, such as the sedating H1-blockers (i.e., diphenhydramine). This effect may be clinically important if a patient is receiving an antihistamine agent for treatment of insomnia. Alternatively, if a patient is receiving an amphetamine for treatment of narcolepsy, the combination with a sedating antihistamine may reverse the action of the amphetamine.
Dexlansoprazole: (Moderate) Use amphetamine; dextroamphetamine and proton pump inhibitors concomitantly with caution. Gastrointestinal alkalinizing agents may increase exposure to amphetamine; dextroamphetamine and exacerbate its actions.
Dextromethorphan; buPROPion: (Moderate) Use extreme caution when coadministering bupropion with other drugs that lower the seizure threshold, such as stimulants including amphetamine; dextroamphetamine. Use low initial doses of bupropion and

increase the dose gradually.
Dextromethorphan; diphenhydrAMINE; Phenylephrine: (Moderate) Amphetamines may pharmacodynamically counteract the sedative properties of some antihistamines, such as the sedating H1-blockers (i.e., diphenhydramine). This effect may be clinically important if a patient is receiving an antihistamine agent for treatment of insomnia. Alternatively, if a patient is receiving an amphetamine for treatment of narcolepsy, the combination with a sedating antihistamine may reverse the action of the amphetamine.
Dextromethorphan; quiNIDine: (Moderate) Warn patients that the risk of amphetamine toxicity may be increased during concurrent use of quinidine, a strong CYP2D6 inhibitor. Amphetamines are partially metabolized by CYP2D6 and have serotonergic properties; inhibition of amphetamine metabolism may increase the risk of serotonin syndrome or other toxicity. If serotonin syndrome occurs, both the amphetamine and CYP2D6 inhibitor should be discontinued and appropriate medical treatment should be implemented.
Diazoxide: (Moderate) Use sympathomimetic agents with caution in patients receiving therapy for hypertension. Patients should be monitored to confirm that the desired antihypertensive effect is achieved. Sympathomimetics can increase blood pressure and heart rate, and antagonize the antihypertensive effects of vasodilators when administered concomitantly. Anginal pain may be induced when coronary insufficiency is present.
Dihydroergotamine: (Contraindicated) Concomitant use of ergotamine with amphetamine or an amphetamine derivative is contraindicated due to the risk for a synergistic increase in blood pressure. Coadministration may also increase the risk for vasospasm which may lead to cerebral or peripheral ischemia.
dilTIAZem: (Minor) Amphetamines increase both systolic and diastolic blood pressure and may counteract the activity of some antihypertensive agents, like calcium-channel blockers. Close monitoring of blood pressure is advised.
dimenhyDRINATE: (Moderate) Amphetamines may pharmacodynamically counteract the sedative properties of some antihistamines, such as the sedating H1-blockers (i.e., diphenhydramine). This effect may be clinically important if a patient is receiving an antihistamine agent for treatment of insomnia. Alternatively, if a patient is receiving an amphetamine for treatment of narcolepsy, the combination with a sedating antihistamine may reverse the action of the amphetamine.
Dipeptidyl Peptidase-4 Inhibitors: (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking dipeptidyl peptidase-4 (DPP-4) inhibitors. Sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short

term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.
diphenhydrAMINE: (Moderate) Amphetamines may pharmacodynamically counteract the sedative properties of some antihistamines, such as the sedating H1-blockers (i.e., diphenhydramine). This effect may be clinically important if a patient is receiving an antihistamine agent for treatment of insomnia. Alternatively, if a patient is receiving an amphetamine for treatment of narcolepsy, the combination with a sedating antihistamine may reverse the action of the amphetamine.
diphenhydrAMINE; Ibuprofen: (Moderate) Amphetamines may pharmacodynamically counteract the sedative properties of some antihistamines, such as the sedating H1-blockers (i.e., diphenhydramine). This effect may be clinically important if a patient is receiving an antihistamine agent for treatment of insomnia. Alternatively, if a patient is receiving an amphetamine for treatment of narcolepsy, the combination with a sedating antihistamine may reverse the action of the amphetamine.
diphenhydrAMINE; Naproxen: (Moderate) Amphetamines may pharmacodynamically counteract the sedative properties of some antihistamines, such as the sedating H1-blockers (i.e., diphenhydramine). This effect may be clinically important if a patient is receiving an antihistamine agent for treatment of insomnia. Alternatively, if a patient is receiving an amphetamine for treatment of narcolepsy, the combination with a sedating antihistamine may reverse the action of the amphetamine.
diphenhydrAMINE; Phenylephrine: (Moderate) Amphetamines may pharmacodynamically counteract the sedative properties of some antihistamines, such as the sedating H1-blockers (i.e., diphenhydramine). This effect may be clinically important if a patient is receiving an antihistamine agent for treatment of insomnia. Alternatively, if a patient is receiving an amphetamine for treatment of narcolepsy, the combination with a sedating antihistamine may reverse the action of the amphetamine.
Dorzolamide; Timolol: (Moderate) Monitor hemodynamic parameters and for loss of efficacy during concomitant sympathomimetic agent and beta-blocker use; dosage adjustments may be necessary. Concomitant use may antagonize the cardiovascular effects of either drug.
Doxazosin: (Minor) Close monitoring of blood pressure or the selection of alternative therapeutic agents may be needed in patients receiving doxazosin and amphetamines. Amphetamines increase both systolic and diastolic blood pressure and may counteract the activity of some antihypertensive agents, such as doxazosin.
Doxepin: (Moderate) Monitor blood pressure, heart rate, and for signs and symptoms of serotonin syndrome, particularly during treatment initiation and dosage increase, during concomitant amphetamine and tricyclic antidepressant use. Adjust doses or use alternative therapy based on clinical response. If serotonin syndrome occurs, discontinue therapy. Concomitant use increases the risk for potentiation of cardiovascular effects and serotonin syndrome. Amphetamines may enhance the

activity of tricyclic antidepressants causing significant and sustained increases in amphetamine concentrations in the brain.
Doxylamine: (Moderate) Amphetamines may pharmacodynamically counteract the sedative properties of some antihistamines, such as the sedating H1-blockers (i.e., diphenhydramine). This effect may be clinically important if a patient is receiving an antihistamine agent for treatment of insomnia. Alternatively, if a patient is receiving an amphetamine for treatment of narcolepsy, the combination with a sedating antihistamine may reverse the action of the amphetamine.
Doxylamine; Pyridoxine: (Moderate) Amphetamines may pharmacodynamically counteract the sedative properties of some antihistamines, such as the sedating H1-blockers (i.e., diphenhydramine). This effect may be clinically important if a patient is receiving an antihistamine agent for treatment of insomnia. Alternatively, if a patient is receiving an amphetamine for treatment of narcolepsy, the combination with a sedating antihistamine may reverse the action of the amphetamine.
droNABinol: (Moderate) Concurrent use of dronabinol, THC with sympathomimetics may result in additive hypertension, tachycardia, and possibly cardiotoxicity. Dronabinol, THC has been associated with occasional hypotension, hypertension, syncope, and tachycardia. In a study of 7 adult males, combinations of IV cocaine and smoked marijuana, 1 g marijuana cigarette, 0 to 2.7% delta-9-THC, increased the heart rate above levels seen with either agent alone, with increases plateauing at 50 bpm.
Dulaglutide: (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking incretin mimetics. Sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.
DULoxetine: (Moderate) Coadministration of amphetamines with serotonin norepinephrine reuptake inhibitors (SNRIs) may increase the risk of serotonin syndrome. At high doses, amphetamines can increase serotonin release and act as serotonin agonists. Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome, particularly during treatment initiation and dose increases. If serotonin syndrome occurs, serotonergic drugs should be discontinued and appropriate medical treatment should be initiated.
Eletriptan: (Moderate) Monitor for signs and symptoms of serotonin syndrome, particularly during treatment initiation and dosage increase, during concomitant serotonin-receptor agonist and amphetamine; dextroamphetamine use. If serotonin syndrome occurs, discontinue therapy. Concomitant use increases the risk for serotonin

syndrome.
Empagliflozin: (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking SGLT2 inhibitors. Sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.
Empagliflozin; Linagliptin: (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking dipeptidyl peptidase-4 (DPP-4) inhibitors. Sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes. (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking SGLT2 inhibitors. Sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.
Empagliflozin; Linagliptin; metFORMIN: (Moderate) Monitor for loss of glycemic control when amphetamines are administered to patients taking antidiabetic agents. Sympathomimetic agents and adrenergic agonists tend to increase blood glucose concentrations when administered systemically. Sympathomimetic agents, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking dipeptidyl peptidase-4 (DPP-4) inhibitors. Sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short

term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes. (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking SGLT2 inhibitors. Sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.
Empagliflozin; metFORMIN: (Moderate) Monitor for loss of glycemic control when amphetamines are administered to patients taking antidiabetic agents. Sympathomimetic agents and adrenergic agonists tend to increase blood glucose concentrations when administered systemically. Sympathomimetic agents, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking SGLT2 inhibitors. Sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.
Enalapril, Enalaprilat: (Minor) Amphetamines increase both systolic and diastolic blood pressure and may counteract the activity of some antihypertensive agents, like angiotensin-converting enzyme inhibitors (ACE inhibitors). Close monitoring of blood pressure is advised.
Enalapril; hydroCHLOROthiazide, HCTZ: (Minor) Amphetamines increase both systolic and diastolic blood pressure and may counteract the activity of some antihypertensive agents, like angiotensin-converting enzyme inhibitors (ACE inhibitors). Close monitoring of blood pressure is advised. (Minor) Amphetamines may counteract the activity of some antihypertensive agents, such as thiazide diuretics. Close monitoring of blood pressure is advised. Thiazide diuretics may also increase and prolong the actions of amphetamines by increasing the urinary pH.
EPINEPHrine: (Moderate) Monitor blood pressure and heart rate during concomitant amphetamine and epinephrine use. Amphetamines may potentiate the pressor effects of epinephrine.
Eplerenone: (Minor) Close monitoring of blood pressure or the selection of alternative

therapeutic agents may be needed in patients receiving eplerenone and amphetamines. Amphetamines increase both systolic and diastolic blood pressure and may counteract the activity of some antihypertensive agents.
Epoprostenol: (Major) Avoid use of sympathomimetic agents with epoprostenol. Sympathomimetics counteract the medications used to stabilize pulmonary hypertension, including epoprostenol. Sympathomimetics can increase blood pressure, increase heart rate, and may cause vasoconstriction resulting in chest pain and shortness of breath in these patients. Patients should be advised to avoid amphetamine drugs, decongestants (including nasal decongestants) and sympathomimetic anorexiants for weight loss, including dietary supplements. Intravenous vasopressors may be used in the emergency management of pulmonary hypertension patients when needed, but hemodynamic monitoring and careful monitoring of cardiac status are needed to avoid ischemia and other complications.
Ergotamine: (Contraindicated) Concomitant use of ergotamine with amphetamine or an amphetamine derivative is contraindicated due to the risk for a synergistic increase in blood pressure. Coadministration may also increase the risk for vasospasm which may lead to cerebral or peripheral ischemia.
Ergotamine; Caffeine: (Contraindicated) Concomitant use of ergotamine with amphetamine or an amphetamine derivative is contraindicated due to the risk for a synergistic increase in blood pressure. Coadministration may also increase the risk for vasospasm which may lead to cerebral or peripheral ischemia. (Moderate) Avoid excessive caffeine intake during use of the amphetamine salts. Caffeine is a CNS-stimulant and such actions are expected to be additive when coadministered with other CNS stimulants or psychostimulants. Excessive caffeine ingestion (via medicines, foods like chocolate, dietary supplements, or beverages including coffee, green tea, other teas, colas) may contribute to side effects like nervousness, irritability, nausea, insomnia, or tremor. Patients should avoid medications and dietary supplements which contain high amounts of caffeine.
Ertugliflozin: (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking SGLT2 inhibitors. Sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.
Ertugliflozin; metFORMIN: (Moderate) Monitor for loss of glycemic control when amphetamines are administered to patients taking antidiabetic agents. Sympathomimetic agents and adrenergic agonists tend to increase blood glucose

concentrations when administered systemically. Sympathomimetic agents, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking SGLT2 inhibitors. Sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.
Ertugliflozin; SITagliptin: (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking dipeptidyl peptidase-4 (DPP-4) inhibitors. Sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes. (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking SGLT2 inhibitors. Sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.
Escitalopram: (Moderate) Coadministration of selective serotonin reuptake inhibitors (SSRIs) like escitalopram with amphetamines may increase the risk of serotonin syndrome. At high doses, amphetamines can increase serotonin release and act as serotonin agonists. Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome, particularly during treatment initiation and dose increases. If serotonin syndrome occurs, serotonergic drugs should be discontinued and appropriate medical treatment should be initiated.
Esketamine: (Major) Closely monitor blood pressure during concomitant use of esketamine and an amphetamine. Coadministration of psychostimulants, such as amphetamines, with esketamine may increase blood pressure, including the possibility of hypertensive crisis.

Eslicarbazepine: (Moderate) Patients who are taking anticonvulsants for epilepsy/seizure control should use amphetamines with caution. Amphetamines may decrease the seizure threshold and may increase the risk of seizures. If seizures occur, amphetamine discontinuation may be necessary. Additionally, amphetamines may delay the intestinal absorption of ethosuximide, ethotoin (hydantoin), phenobarbital, and phenytoin, the extent of absorption of these seizure medications is not known to be affected.
Esmolol: (Moderate) Monitor hemodynamic parameters and for loss of efficacy during concomitant sympathomimetic agent and beta-blocker use; dosage adjustments may be necessary. Concomitant use may antagonize the cardiovascular effects of either drug.
Esomeprazole: (Moderate) Use amphetamine; dextroamphetamine and proton pump inhibitors concomitantly with caution. Gastrointestinal alkalinizing agents may increase exposure to amphetamine; dextroamphetamine and exacerbate its actions.
Ethacrynic Acid: (Minor) Amphetamine and Dextroamphetamine may increase both systolic and diastolic blood pressure and may counteract the activity of some antihypertensive agents, such as loop diuretics. Close monitoring of blood pressure is advised.
Ethanol: (Major) Advise patients to avoid alcohol while taking some dosage forms (e.g., Mydayis extended-release capsules) of amphetamine/dextroamphetamine salts. Consumption of alcohol while taking such dosage forms may result in a more rapid release of the dose of mixed amphetamine salts. Such effects may potentially lead to serious side effects such as acute anxiety, problems with sleep, or increases in heart rate or blood pressure that may lead to heart problems or stroke.
Ethiodized Oil: (Major) Use of medications that lower the seizure threshold should be carefully evaluated when considering the use of intrathecal radiopaque contrast agents. Amphetamines should be discontinued at least 48 hours before myelography and should not be resumed for at least 24 hours postprocedure.
Ethosuximide: (Moderate) Patients who are taking anticonvulsants for epilepsy/seizure control should use amphetamines with caution. Amphetamines may decrease the seizure threshold and may increase the risk of seizures. The amphetamines may also delay the intestinal absorption of ethosuximide; the extent of absorption of these seizure medications is not known to be affected.
Etomidate: (Major) Inhalational general anesthetics may sensitize the myocardium to the effects of dextroamphetamine. Dosages of the amphetamines should be substantially reduced prior to surgery, and caution should be observed with concurrent use of anesthetics.
Exenatide: (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking incretin mimetics. Sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic

medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.
Famotidine: (Moderate) Use amphetamine; dextroamphetamine and H2-blockers concomitantly with caution. Gastrointestinal alkalinizing agents may increase exposure to amphetamine; dextroamphetamine and exacerbate its actions.
Felodipine: (Minor) Amphetamines increase both systolic and diastolic blood pressure and may counteract the activity of some antihypertensive agents, like calcium-channel blockers. Close monitoring of blood pressure is advised.
Fenfluramine: (Moderate) Use fenfluramine and amphetamines with caution due to an increased risk of serotonin syndrome. Monitor patients for the emergence of serotonin syndrome. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs.
Fenoldopam: (Moderate) Use sympathomimetic agents with caution in patients receiving therapy for hypertension. Patients should be monitored to confirm that the desired antihypertensive effect is achieved. Sympathomimetics can increase blood pressure and heart rate, and antagonize the antihypertensive effects of vasodilators when administered concomitantly. Anginal pain may be induced when coronary insufficiency is present.
fentaNYL: (Moderate) If concomitant use of fentanyl and amphetamines is warranted, monitor patients for the emergence of serotonin syndrome. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs. The concomitant use of opioids with other drugs that affect the serotonergic neurotransmitter system has resulted in serotonin syndrome.
FLUoxetine: (Moderate) Monitor for signs and symptoms of serotonin syndrome, particularly during treatment initiation and dosage increase, during concomitant amphetamine and fluoxetine use. If serotonin syndrome occurs, discontinue therapy. Concomitant use increases the risk for serotonin syndrome.
Fluticasone; Salmeterol: (Moderate) Monitor blood pressure and heart rate during concomitant amphetamine; dextroamphetamine and salmeterol use. Concomitant use may potentiate sympathetic effects.
Fluticasone; Umeclidinium; Vilanterol: (Moderate) Administer sympathomimetics with caution with beta-agonists such as vilanterol. The cardiovascular effects of beta-2 agonists may be potentiated by concomitant use. Monitor the patient for tremors, nervousness, increased heart rate, or other additive side effects.
Fluticasone; Vilanterol: (Moderate) Administer sympathomimetics with caution with beta-agonists such as vilanterol. The cardiovascular effects of beta-2 agonists may be potentiated by concomitant use. Monitor the patient for tremors, nervousness, increased heart rate, or other additive side effects.

fluvoxaMINE: (Moderate) Coadministration of selective serotonin reuptake inhibitors (SSRIs) like fluvoxamine with amphetamines may increase the risk of serotonin syndrome. At high doses, amphetamines can increase serotonin release and act as serotonin agonists. Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome, particularly during treatment initiation and dose increases. If serotonin syndrome occurs, serotonergic drugs should be discontinued and appropriate medical treatment should be initiated.
Food: (Moderate) In general, food does not significantly interact with the amphetamine stimulants, a dose may be taken with or without food. However, certain gastrointestinal acidifying agents (e.g., certain fruit juices, etc.) can lower the oral absorption of amphetamines. To ensure proper absorption, it may be prudent for the patient to avoid citrus fruits and citrus juices 1 hour before a dose, at the time of dosing, and for the 1 hour following a dose. In addition, the excretion of amphetamines is increased in acidic urine and decreased in alkaline urine. Foods that acidify the urine, such as cranberry juice, orange juice, or those that contain vitamin C (ascorbic acid) may increase amphetamine renal excretion. Conversely, foods that alkalinize the urine, such as beets, dairy products, kale, spinach may slightly slow urinary excretion of amphetamines. Patients should not significantly alter their diets, however, as these changes in urinary pH from foods are not expected to be clinically significant for most patients. (Minor) In general, food does not significantly interact with the amphetamine stimulants, a dose may be taken with or without food. Foods that alkalinize the urine, such as beets, dairy products, kale, spinach may slightly slow urinary excretion of amphetamines. Patients should not significantly alter their diets, however, as these alkaline changes in urinary pH from foods are not expected to be clinically significant for most patients.
Formoterol: (Moderate) Monitor blood pressure and heart rate during concomitant amphetamine; dextroamphetamine and formoterol use. Concomitant use may potentiate sympathetic effects.
Formoterol; Mometasone: (Moderate) Monitor blood pressure and heart rate during concomitant amphetamine; dextroamphetamine and formoterol use. Concomitant use may potentiate sympathetic effects.
Fosinopril: (Minor) Amphetamines increase both systolic and diastolic blood pressure and may counteract the activity of some antihypertensive agents, like angiotensin-converting enzyme inhibitors (ACE inhibitors). Close monitoring of blood pressure is advised.
Fosinopril; hydroCHLOROthiazide, HCTZ: (Minor) Amphetamines increase both systolic and diastolic blood pressure and may counteract the activity of some antihypertensive agents, like angiotensin-converting enzyme inhibitors (ACE inhibitors). Close monitoring of blood pressure is advised. (Minor) Amphetamines may counteract the activity of some antihypertensive agents, such as thiazide diuretics. Close monitoring of blood pressure is advised. Thiazide diuretics may also increase and prolong the actions of

amphetamines by increasing the urinary pH.
Frovatriptan: (Moderate) Monitor for signs and symptoms of serotonin syndrome, particularly during treatment initiation and dosage increase, during concomitant serotonin-receptor agonist and amphetamine; dextroamphetamine use. If serotonin syndrome occurs, discontinue therapy. Concomitant use increases the risk for serotonin syndrome.
Furosemide: (Minor) Amphetamine and Dextroamphetamine may increase both systolic and diastolic blood pressure and may counteract the activity of some antihypertensive agents, such as loop diuretics. Close monitoring of blood pressure is advised.
Gepirone: (Moderate) Monitor for serotonin syndrome if concomitant use of gepirone and amphetamines is necessary. Both medications affect the serotonergic neurotransmitter system; concomitant use increases the risk for serotonin syndrome.
Glimepiride: (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking sulfonylureas. Sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.
glipiZIDE: (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking sulfonylureas. Sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.
glipiZIDE; metFORMIN: (Moderate) Monitor for loss of glycemic control when amphetamines are administered to patients taking antidiabetic agents. Sympathomimetic agents and adrenergic agonists tend to increase blood glucose concentrations when administered systemically. Sympathomimetic agents, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking sulfonylureas. Sympathomimetics, through stimulation of alpha- and beta- receptors,

increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.
glyBURIDE: (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking sulfonylureas. Sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.
glyBURIDE; metFORMIN: (Moderate) Monitor for loss of glycemic control when amphetamines are administered to patients taking antidiabetic agents. Sympathomimetic agents and adrenergic agonists tend to increase blood glucose concentrations when administered systemically. Sympathomimetic agents, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking sulfonylureas. Sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.
Glycopyrrolate; Formoterol: (Moderate) Monitor blood pressure and heart rate during concomitant amphetamine; dextroamphetamine and formoterol use. Concomitant use may potentiate sympathetic effects.
guanFACINE: (Moderate) Sympathomimetic agents, such as amphetamines, may increase blood pressure and reduce the antihypertensive effects of antihypertensive agents, such as guanfacine. Monitor blood pressure and heart rate periodically when prescribed together. Guanfacine may be used adjunctively to psychostimulants such as amphetamines in the treatment of attention deficit hyperactivity disorder (ADHD). Pharmacokinetic studies reveal that guanfacine does not influence lisdexamfetamine pharmacokinetics and lisdexamfetamine does not affect guanfacine pharmacokinetics. No dosage adjustments are required when guanfacine and amphetamines are used

together for ADHD. Monitor heart rate, blood pressure and for sedation during ADHD treatment.
H2-blockers: (Moderate) Use amphetamine; dextroamphetamine and H2-blockers concomitantly with caution. Gastrointestinal alkalinizing agents may increase exposure to amphetamine; dextroamphetamine and exacerbate its actions.
Homatropine; HYDROcodone: (Moderate) If concomitant use of hydrocodone and amphetamines is warranted, monitor patients for the emergence of serotonin syndrome. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs. The concomitant use of opioids with other drugs that affect the serotonergic neurotransmitter system has resulted in serotonin syndrome.
hydrALAZINE: (Moderate) Use sympathomimetic agents with caution in patients receiving therapy for hypertension. Patients should be monitored to confirm that the desired antihypertensive effect is achieved. Sympathomimetics can increase blood pressure and heart rate, and antagonize the antihypertensive effects of vasodilators when administered concomitantly. Anginal pain may be induced when coronary insufficiency is present.
hydrALAZINE; Isosorbide Dinitrate, ISDN: (Moderate) Sympathomimetics can antagonize the antianginal effects of nitrates, and can increase blood pressure and/or heart rate. Anginal pain may be induced when coronary insufficiency is present. (Moderate) Use sympathomimetic agents with caution in patients receiving therapy for hypertension. Patients should be monitored to confirm that the desired antihypertensive effect is achieved. Sympathomimetics can increase blood pressure and heart rate, and antagonize the antihypertensive effects of vasodilators when administered concomitantly. Anginal pain may be induced when coronary insufficiency is present.
hydroCHLOROthiazide, HCTZ: (Minor) Amphetamines may counteract the activity of some antihypertensive agents, such as thiazide diuretics. Close monitoring of blood pressure is advised. Thiazide diuretics may also increase and prolong the actions of amphetamines by increasing the urinary pH.
hydroCHLOROthiazide, HCTZ; Moexipril: (Minor) Amphetamines increase both systolic and diastolic blood pressure and may counteract the activity of some antihypertensive agents, like angiotensin-converting enzyme inhibitors (ACE inhibitors). Close monitoring of blood pressure is advised. (Minor) Amphetamines may counteract the activity of some antihypertensive agents, such as thiazide diuretics. Close monitoring of blood pressure is advised. Thiazide diuretics may also increase and prolong the actions of amphetamines by increasing the urinary pH.
HYDROcodone: (Moderate) If concomitant use of hydrocodone and amphetamines is warranted, monitor patients for the emergence of serotonin syndrome. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs. The concomitant use of opioids with other drugs that affect the serotonergic neurotransmitter system has resulted in serotonin syndrome.

HYDROcodone; Ibuprofen: (Moderate) If concomitant use of hydrocodone and amphetamines is warranted, monitor patients for the emergence of serotonin syndrome. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs. The concomitant use of opioids with other drugs that affect the serotonergic neurotransmitter system has resulted in serotonin syndrome.
HYDROmorphone: (Moderate) If concomitant use of hydromorphone and amphetamines is warranted, monitor patients for the emergence of serotonin syndrome. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs. The concomitant use of opioids with other drugs that affect the serotonergic neurotransmitter system has resulted in serotonin syndrome.
hydrOXYzine: (Moderate) Amphetamines may pharmacodynamically counteract the sedative properties of some antihistamines, such as the sedating H1-blockers (i.e., diphenhydramine). This effect may be clinically important if a patient is receiving an antihistamine agent for treatment of insomnia. Alternatively, if a patient is receiving an amphetamine for treatment of narcolepsy, the combination with a sedating antihistamine may reverse the action of the amphetamine.
Hyoscyamine; Methenamine; Methylene Blue; Phenyl Salicylate; Sodium Biphosphate: (Contraindicated) Amphetamines should not be administered during or within 14 days after the use of methylene blue. Methylene blue is a potent, reversible monoamine oxidase inhibitor (MAOI) which can prolong and intensify the cardiac stimulation and vasopressor effects of amphetamines, potentially resulting in hypertensive crisis. Methylene blue also has the potential to interact with serotonergic agents, such as amphetamines, which may increase the risk for serotonin syndrome. Serotonin syndrome is characterized by 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, gastrointestinal symptoms (e.g., nausea, vomiting, diarrhea), and in rare instances, death. Cases of serotonin syndrome have been reported, primarily following administration of standard infusions of methylene blue (1 to 8 mg/kg) as a visualizing agent in parathyroid surgery, in patients receiving selective serotonin reuptake inhibitors, serotonin/norepinephrine reuptake inhibitors, or clomipramine. It is not known if patients receiving other serotonergic psychiatric agents, such as amphetamines, with intravenous methylene blue are at a comparable risk or if methylene blue administered by other routes (e.g., orally, local injection) or in doses less than 1 mg/kg IV can produce a similar outcome. Published interaction reports between intravenously administered methylene blue and serotonergic psychiatric agents have documented symptoms including lethargy, confusion, delirium, agitation, aggression, obtundation, myoclonus, expressive aphasia, hypertonia, pyrexia, elevated blood pressure, seizures, and/or coma. (Major) Urinary acidifying agents, such as ammonium chloride, phosphorus salts, and methenamine

salts (e.g., methenamine; sodium acid phosphate), reduce the tubular reabsorption of amphetamines. As a result, amphetamine clearance is accelerated and the duration of effect is reduced. Combination therapy should be avoided if possible.
Ibritumomab Tiuxetan: (Moderate) Monitor for an increase in the incidence and severity of amphetamine-related adverse effects during concomitant use of urinary alkalinizing agents. Increasing urine pH may increase amphetamine exposure by reducing urinary excretion of amphetamine. A urine pH more than 7.5 has been observed to increase the half-life of amphetamine from 8 to 10.5 hours to 16 to 31 hours when compared to a pH less than 6. Additionally, a urine pH more than 8 has been observed to reduce the amount of amphetamine excreted in the urine over 16 hours to less than 3% of the original dose; a 5-fold reduction compared to controls.
Ibuprofen; Famotidine: (Moderate) Use amphetamine; dextroamphetamine and H2-blockers concomitantly with caution. Gastrointestinal alkalinizing agents may increase exposure to amphetamine; dextroamphetamine and exacerbate its actions.
Iloprost: (Major) Avoid use of sympathomimetic agents with iloprost. Sympathomimetics counteract the medications used to stabilize pulmonary hypertension, including iloprost. Sympathomimetics can increase blood pressure, increase heart rate, and may cause vasoconstriction resulting in chest pain and shortness of breath in these patients. Patients should be advised to avoid amphetamine drugs, decongestants (including nasal decongestants) and sympathomimetic anorexiants for weight loss, including dietary supplements. Intravenous vasopressors may be used in the emergency management of pulmonary hypertension patients when needed, but hemodynamic monitoring and careful monitoring of cardiac status are needed to avoid ischemia and other complications.
Imipramine: (Moderate) Monitor blood pressure, heart rate, and for signs and symptoms of serotonin syndrome, particularly during treatment initiation and dosage increase, during concomitant amphetamine and tricyclic antidepressant use. Adjust doses or use alternative therapy based on clinical response. If serotonin syndrome occurs, discontinue therapy. Concomitant use increases the risk for potentiation of cardiovascular effects and serotonin syndrome. Amphetamines may enhance the activity of tricyclic antidepressants causing significant and sustained increases in amphetamine concentrations in the brain.
Incretin Mimetics: (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking incretin mimetics. Sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for

diabetes.
Indacaterol; Glycopyrrolate: (Moderate) Administer sympathomimetics with caution with beta-agonists such as indacaterol. The cardiovascular effects of beta-2 agonists may be potentiated by concomitant use. Monitor the patient for tremors, nervousness, increased heart rate, or other additive side effects.
Indapamide: (Moderate) Indapamide may increase blood levels and therefore potentiate the actions of amphetamines. Thiazide diuretics and related drugs like indapamide may increase urinary pH, acting as a urinary alkalinizer, thus reducing urinary excretion and increasing blood concentrations of the amphetamine. Co-administration of amphetamines and urinary alkalinizing agents should be avoided if possible. If needed, monitor for common amphetamine side effects, including decreased appetite, anxiety, dizziness, dry mouth, irritability, insomnia, nausea, increased blood pressure or increased heart rate.
Insulin Aspart: (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking insulin. Sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.
Insulin Aspart; Insulin Aspart Protamine: (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking insulin. Sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.
Insulin Degludec: (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking insulin. Sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.

Insulin Degludec; Liraglutide: (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking incretin mimetics. Sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes. (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking insulin. Sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.

Insulin Detemir: (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking insulin. Sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.

Insulin Glargine: (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking insulin. Sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.

Insulin Glargine; Lixisenatide: (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking incretin mimetics. Sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion.

Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes. (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking insulin. Sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.
Insulin Glulisine: (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking insulin. Sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.
Insulin Lispro: (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking insulin. Sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.
Insulin Lispro; Insulin Lispro Protamine: (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking insulin. Sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.
Insulin, Inhaled: (Moderate) Sympathomimetic agents tend to increase blood glucose

concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking insulin.
Sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.
Insulins: (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking insulin.
Sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.
Iobenguane I 131: (Major) Discontinue sympathomimetics for at least 5 half-lives before the administration of the dosimetry dose or a therapeutic dose of iobenguane I-131. Do not restart sympathomimetics until at least 7 days after each iobenguane I-131 dose. Drugs that reduce catecholamine uptake or deplete catecholamine stores, such as sympathomimetics, may interfere with iobenguane I-131 uptake into cells and interfere with dosimetry calculations resulting in altered iobenguane I-131 efficacy.
Iodixanol: (Major) Use of medications that lower the seizure threshold should be carefully evaluated when considering the use of intrathecal radiopaque contrast agents. Amphetamines should be discontinued at least 48 hours before myelography and should not be resumed for at least 24 hours postprocedure.
Ioflupane I 123: (Major) Hold amphetamines for 7 days, or at least 5 medication half-lives, prior to performing dopamine transporter (DAT) imaging with radiolabeled ioflupane. Amphetamines bind to the dopamine transporter which may interfere with striatal tracer binding and increase the risk for a false-positive scan.
Iohexol: (Major) Use of medications that lower the seizure threshold should be carefully evaluated when considering the use of intrathecal radiopaque contrast agents. Amphetamines should be discontinued at least 48 hours before myelography and should not be resumed for at least 24 hours postprocedure.
Iomeprol: (Major) Use of medications that lower the seizure threshold should be carefully evaluated when considering the use of intrathecal radiopaque contrast agents. Amphetamines should be discontinued at least 48 hours before myelography and should not be resumed for at least 24 hours postprocedure.
Iopamidol: (Major) Use of medications that lower the seizure threshold should be

carefully evaluated when considering the use of intrathecal radiopaque contrast agents. Amphetamines should be discontinued at least 48 hours before myelography and should not be resumed for at least 24 hours postprocedure.
Iopromide: (Major) Use of medications that lower the seizure threshold should be carefully evaluated when considering the use of intrathecal radiopaque contrast agents. Amphetamines should be discontinued at least 48 hours before myelography and should not be resumed for at least 24 hours postprocedure.
Ioversol: (Major) Use of medications that lower the seizure threshold should be carefully evaluated when considering the use of intrathecal radiopaque contrast agents. Amphetamines should be discontinued at least 48 hours before myelography and should not be resumed for at least 24 hours postprocedure.
Ipratropium; Albuterol: (Moderate) Monitor blood pressure and heart rate during concomitant albuterol and amphetamine; dextroamphetamine use. Concomitant use may potentiate sympathetic effects.
Irbesartan: (Minor) Amphetamines increase both systolic and diastolic blood pressure and may counteract the activity of some antihypertensive agents, such as angiotensin II receptor antagonists. Close monitoring of blood pressure is advised.
Irbesartan; hydroCHLOROthiazide, HCTZ: (Minor) Amphetamines increase both systolic and diastolic blood pressure and may counteract the activity of some antihypertensive agents, such as angiotensin II receptor antagonists. Close monitoring of blood pressure is advised. (Minor) Amphetamines may counteract the activity of some antihypertensive agents, such as thiazide diuretics. Close monitoring of blood pressure is advised. Thiazide diuretics may also increase and prolong the actions of amphetamines by increasing the urinary pH.
Isocarboxazid: (Contraindicated) In general, sympathomimetics should be avoided in patients receiving MAOIs due to an increased risk of hypertensive crisis. This applies to sympathomimetics including stimulants for ADHD, narcolepsy or weight loss, nasal, oral, and ophthalmic decongestants and cold products, and respiratory sympathomimetics (e.g., beta agonist drugs). Some local anesthetics also contain a sympathomimetic (e.g., epinephrine). In general, medicines containing sympathomimetic agents should not be used concurrently with MAOIs or within 14 days before or after their use.
Isoflurane: (Major) Inhalational general anesthetics (e.g., enflurane, halothane, isoflurane, and methoxyflurane) may sensitize the myocardium to the effects of stimulants. Dosages of the amphetamines should be substantially reduced prior to surgery, and caution should be observed with concurrent use of anesthetics.
Isophane Insulin (NPH): (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking insulin. Sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic

medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.
Isosorbide Dinitrate, ISDN: (Moderate) Sympathomimetics can antagonize the antianginal effects of nitrates, and can increase blood pressure and/or heart rate. Anginal pain may be induced when coronary insufficiency is present.
Isosorbide Mononitrate: (Moderate) Sympathomimetics can antagonize the antianginal effects of nitrates, and can increase blood pressure and/or heart rate. Anginal pain may be induced when coronary insufficiency is present.
Isosulfan Blue: (Major) Use of medications that lower the seizure threshold should be carefully evaluated when considering the use of intrathecal radiopaque contrast agents. Amphetamines should be discontinued at least 48 hours before myelography and should not be resumed for at least 24 hours postprocedure.
Isradipine: (Minor) Amphetamines increase both systolic and diastolic blood pressure and may counteract the activity of some antihypertensive agents, like calcium-channel blockers. Close monitoring of blood pressure is advised.
Ketamine: (Moderate) Closely monitor vital signs when ketamine and amphetamine; dextroamphetamine salts are coadministered; consider dose adjustment individualized to the patient's clinical situation. Amphetamine; dextroamphetamine salts may enhance the sympathomimetic effects of ketamine.
Labetalol: (Moderate) Monitor hemodynamic parameters and for loss of efficacy during concomitant sympathomimetic agent and beta-blocker use; dosage adjustments may be necessary. Concomitant use may antagonize the cardiovascular effects of either drug.
Landiolol: (Moderate) Monitor hemodynamic parameters and for loss of efficacy during concomitant sympathomimetic agent and beta-blocker use; dosage adjustments may be necessary. Concomitant use may antagonize the cardiovascular effects of either drug.
Lansoprazole: (Moderate) Use amphetamine; dextroamphetamine and proton pump inhibitors concomitantly with caution. Gastrointestinal alkalinizing agents may increase exposure to amphetamine; dextroamphetamine and exacerbate its actions.
Lansoprazole; Amoxicillin; Clarithromycin: (Moderate) Use amphetamine; dextroamphetamine and proton pump inhibitors concomitantly with caution. Gastrointestinal alkalinizing agents may increase exposure to amphetamine; dextroamphetamine and exacerbate its actions.
Lasmiditan: (Moderate) Serotonin syndrome may occur during coadministration of lasmiditan and amphetamines. Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome particularly after a dose increase or the addition of other serotonergic medications to an existing regimen. Discontinue all serotonergic agents if serotonin syndrome occurs and implement appropriate medical management.

Levalbuterol: (Moderate) Monitor blood pressure and heart rate during concomitant albuterol and amphetamine; dextroamphetamine use. Concomitant use may potentiate sympathetic effects.
Levamlodipine: (Minor) Amphetamines increase both systolic and diastolic blood pressure and may counteract the activity of some antihypertensive agents, like calcium-channel blockers. Close monitoring of blood pressure is advised.
Levobunolol: (Moderate) Monitor hemodynamic parameters and for loss of efficacy during concomitant sympathomimetic agent and beta-blocker use; dosage adjustments may be necessary. Concomitant use may antagonize the cardiovascular effects of either drug.
Levomilnacipran: (Moderate) Coadministration of amphetamines with serotonin norepinephrine reuptake inhibitors (SNRIs) may increase the risk of serotonin syndrome. At high doses, amphetamines can increase serotonin release and act as serotonin agonists. Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome, particularly during treatment initiation and dose increases. If serotonin syndrome occurs, serotonergic drugs should be discontinued and appropriate medical treatment should be initiated.
Levorphanol: (Moderate) If concomitant use of levorphanol and amphetamines is warranted, monitor patients for the emergence of serotonin syndrome. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs. The concomitant use of opioids with other drugs that affect the serotonergic neurotransmitter system has resulted in serotonin syndrome.
Levothyroxine: (Moderate) Monitor hemodynamic parameters during concomitant sympathomimetic agent and thyroid hormone use; dosage adjustments may be necessary. Concomitant use may increase the effects of sympathomimetics or thyroid hormone.
Levothyroxine; Liothyronine (Porcine): (Moderate) Monitor hemodynamic parameters during concomitant sympathomimetic agent and thyroid hormone use; dosage adjustments may be necessary. Concomitant use may increase the effects of sympathomimetics or thyroid hormone.
Lidocaine; EPINEPHrine: (Moderate) Monitor blood pressure and heart rate during concomitant amphetamine and epinephrine use. Amphetamines may potentiate the pressor effects of epinephrine.
Linagliptin: (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking dipeptidyl peptidase-4 (DPP-4) inhibitors. Sympathomimetics, through stimulation of alpha- and beta-receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term,

limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.
Linagliptin; metFORMIN: (Moderate) Monitor for loss of glycemic control when amphetamines are administered to patients taking antidiabetic agents. Sympathomimetic agents and adrenergic agonists tend to increase blood glucose concentrations when administered systemically. Sympathomimetic agents, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking dipeptidyl peptidase-4 (DPP-4) inhibitors. Sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.
Linezolid: (Contraindicated) Amphetamines should not be administered during or within 14 days after the use of linezolid. Linezolid possesses MAO-inhibiting activity and can prolong and intensify the cardiac stimulation and vasopressor effects of the amphetamines, potentially resulting in hypertensive crisis. Linezolid also has the potential to interact with serotonergic agents, such as amphetamines, which may increase the risk for serotonin syndrome. Serotonin syndrome is characterized by 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, gastrointestinal symptoms (e.g., nausea, vomiting, diarrhea), and in rare instances, death. If serotonin syndrome occurs, discontinue serotonergic drugs and institute appropriate medical management.
Liothyronine: (Moderate) Monitor hemodynamic parameters during concomitant sympathomimetic agent and thyroid hormone use; dosage adjustments may be necessary. Concomitant use may increase the effects of sympathomimetics or thyroid hormone.
Liraglutide: (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking incretin mimetics. Sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3

days) as an alternative to systemic decongestants in patients taking medications for diabetes.
Lisinopril: (Minor) Amphetamines increase both systolic and diastolic blood pressure and may counteract the activity of some antihypertensive agents, like angiotensin-converting enzyme inhibitors (ACE inhibitors). Close monitoring of blood pressure is advised.
Lisinopril; hydroCHLOROthiazide, HCTZ: (Minor) Amphetamines increase both systolic and diastolic blood pressure and may counteract the activity of some antihypertensive agents, like angiotensin-converting enzyme inhibitors (ACE inhibitors). Close monitoring of blood pressure is advised. (Minor) Amphetamines may counteract the activity of some antihypertensive agents, such as thiazide diuretics. Close monitoring of blood pressure is advised. Thiazide diuretics may also increase and prolong the actions of amphetamines by increasing the urinary pH.
Lithium: (Moderate) Coadministration of amphetamines and lithium may increase the risk of serotonin syndrome. At high doses, amphetamines can increase serotonin release, as well as act as serotonin agonists. Lithium has central serotonergic effects. Inform patients of the possible increased risk and monitor for serotonin syndrome, particularly during treatment initiation, after a dose increase, or the addition of other serotonergic medications. Discontinue all serotonergic agents if serotonin syndrome occurs and implement appropriate medical management.
Lixisenatide: (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking incretin mimetics. Sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.
Loop diuretics: (Minor) Amphetamine and Dextroamphetamine may increase both systolic and diastolic blood pressure and may counteract the activity of some antihypertensive agents, such as loop diuretics. Close monitoring of blood pressure is advised.
Lopinavir; Ritonavir: (Moderate) Warn patients that the risk of amphetamine toxicity may be increased during concurrent use of ritonavir, a strong CYP2D6 inhibitor. Amphetamines are partially metabolized by CYP2D6 and have serotonergic properties; inhibition of amphetamine metabolism may increase the risk of serotonin syndrome or other toxicity. If serotonin syndrome occurs, both the amphetamine and CYP2D6 inhibitor should be discontinued and appropriate medical treatment should be implemented.

Losartan: (Minor) Amphetamines increase both systolic and diastolic blood pressure and may counteract the activity of some antihypertensive agents, such as angiotensin II receptor antagonists. Close monitoring of blood pressure is advised.
Losartan; hydroCHLOROthiazide, HCTZ: (Minor) Amphetamines increase both systolic and diastolic blood pressure and may counteract the activity of some antihypertensive agents, such as angiotensin II receptor antagonists. Close monitoring of blood pressure is advised. (Minor) Amphetamines may counteract the activity of some antihypertensive agents, such as thiazide diuretics. Close monitoring of blood pressure is advised. Thiazide diuretics may also increase and prolong the actions of amphetamines by increasing the urinary pH.
Loxapine: (Major) Concurrent use of antipsychotics and amphetamines should generally be avoided. Antipsychotics and amphetamines may interact pharmacodynamically to diminish the therapeutic effects of either agent through opposing effects on dopamine. Amphetamines are thought to block central dopamine reuptake, which has the potential to exacerbate psychosis, and antipsychotics, which are central dopamine antagonists, may diminish the effectiveness of amphetamines.
Lurasidone: (Major) Concurrent use of antipsychotics and amphetamines should generally be avoided. Antipsychotics and amphetamines may interact pharmacodynamically to diminish the therapeutic effects of either agent through opposing effects on dopamine. Amphetamines are thought to block central dopamine reuptake, which has the potential to exacerbate psychosis, and antipsychotics, which are central dopamine antagonists, may diminish the effectiveness of amphetamines.
Macitentan: (Major) Avoid use of sympathomimetic agents with macitentan. Sympathomimetics counteract the medications used to stabilize pulmonary hypertension, including macitentan. Sympathomimetics can increase blood pressure, increase heart rate, and may cause vasoconstriction resulting in chest pain and shortness of breath in these patients. Patients should be advised to avoid amphetamine drugs, decongestants (including nasal decongestants) and sympathomimetic anorexiants for weight loss, including dietary supplements. Intravenous vasopressors may be used in the emergency management of pulmonary hypertension patients when needed, but hemodynamic monitoring and careful monitoring of cardiac status are needed to avoid ischemia and other complications.
Macitentan; Tadalafil: (Major) Avoid use of sympathomimetic agents with macitentan. Sympathomimetics counteract the medications used to stabilize pulmonary hypertension, including macitentan. Sympathomimetics can increase blood pressure, increase heart rate, and may cause vasoconstriction resulting in chest pain and shortness of breath in these patients. Patients should be advised to avoid amphetamine drugs, decongestants (including nasal decongestants) and sympathomimetic anorexiants for weight loss, including dietary supplements. Intravenous vasopressors may be used in the emergency management of pulmonary hypertension patients when

needed, but hemodynamic monitoring and careful monitoring of cardiac status are needed to avoid ischemia and other complications.
Magnesium Hydroxide: (Minor) Monitor for an increase in amphetamine-related adverse effects during concomitant antacid use. Increasing gastric or urine pH may increase amphetamine exposure and the risk for side effects in some patients. As antacids have rarely been observed to increase gastric or urinary pH above 6.5, antacid-related pH changes may be insufficient to warrant clinical concern in most patients.
Magnesium Salts: (Minor) Monitor for an increase in amphetamine-related adverse effects during concomitant antacid use. Increasing gastric or urine pH may increase amphetamine exposure and the risk for side effects in some patients. As antacids have rarely been observed to increase gastric or urinary pH above 6.5, antacid-related pH changes may be insufficient to warrant clinical concern in most patients.
Maprotiline: (Moderate) Use maprotiline and sympathomimetics together with caution and close clinical monitoring. Regularly assess blood pressure, heart rate, the efficacy of treatment, and the emergence of sympathomimetic/adrenergic adverse events. Carefully adjust dosages as clinically indicated. Maprotiline has pharmacologic activity similar to tricyclic antidepressant agents and may cause additive sympathomimetic effects when combined with agents with adrenergic/sympathomimetic activity.
Mecamylamine: (Major) The cardiovascular effects of sympathomimetics may reduce the antihypertensive effects produced by mecamylamine. Close monitoring of blood pressure or the selection of alternative therapeutic agents may be needed.
Meclizine: (Moderate) Amphetamines may pharmacodynamically counteract the sedative properties of some antihistamines, such as the sedating H1-blockers (i.e., diphenhydramine). This effect may be clinically important if a patient is receiving an antihistamine agent for treatment of insomnia. Alternatively, if a patient is receiving an amphetamine for treatment of narcolepsy, the combination with a sedating antihistamine may reverse the action of the amphetamine.
Meglitinides: (Moderate) Sympathomimetic agents and adrenergic agonists tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when pseudoephedrine, phenylephrine, and other sympathomimetics are administered to patients taking antidiabetic agents. Epinephrine and other sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.
Meloxicam; Rizatriptan: (Moderate) Monitor for signs and symptoms of serotonin syndrome, particularly during treatment initiation and dosage increase, during concomitant serotonin-receptor agonist and amphetamine; dextroamphetamine use. If

serotonin syndrome occurs, discontinue therapy. Concomitant use increases the risk for serotonin syndrome.
Meperidine: (Moderate) If concomitant use of meperidine and amphetamines is warranted, monitor patients for the emergence of serotonin syndrome. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs. The concomitant use of opioids with other drugs that affect the serotonergic neurotransmitter system has resulted in serotonin syndrome.
Metaproterenol: (Major) Caution and close observation should also be used when metaproterenol is used concurrently with other adrenergic sympathomimetics, administered by any route, to avoid potential for increased cardiovascular effects.
metFORMIN: (Moderate) Monitor for loss of glycemic control when amphetamines are administered to patients taking antidiabetic agents. Sympathomimetic agents and adrenergic agonists tend to increase blood glucose concentrations when administered systemically. Sympathomimetic agents, through stimulation of alpha- and beta-receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells.
metFORMIN; sAXagliptin: (Moderate) Monitor for loss of glycemic control when amphetamines are administered to patients taking antidiabetic agents. Sympathomimetic agents and adrenergic agonists tend to increase blood glucose concentrations when administered systemically. Sympathomimetic agents, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking dipeptidyl peptidase-4 (DPP-4) inhibitors. Sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.
metFORMIN; SITagliptin: (Moderate) Monitor for loss of glycemic control when amphetamines are administered to patients taking antidiabetic agents. Sympathomimetic agents and adrenergic agonists tend to increase blood glucose concentrations when administered systemically. Sympathomimetic agents, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking dipeptidyl

peptidase-4 (DPP-4) inhibitors. Sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.
Methadone: (Moderate) If concomitant use of methadone and amphetamines is warranted, monitor patients for the emergence of serotonin syndrome. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs. The concomitant use of opioids with other drugs that affect the serotonergic neurotransmitter system has resulted in serotonin syndrome.
methazolAMIDE: (Moderate) Urinary alkalinizers, such as methazolamide, result in decreased renal excretion of amphetamines. Monitor for amphetamine-related side effects. Avoid concomitant use in amphetamine overdose situations.
Methenamine: (Major) Urinary acidifying agents, such as ammonium chloride, phosphorus salts, and methenamine salts (e.g., methenamine; sodium acid phosphate), reduce the tubular reabsorption of amphetamines. As a result, amphetamine clearance is accelerated and the duration of effect is reduced. Combination therapy should be avoided if possible.
Methenamine; Sodium Acid Phosphate; Methylene Blue; Hyoscyamine: (Contraindicated) Amphetamines should not be administered during or within 14 days after the use of methylene blue. Methylene blue is a potent, reversible monoamine oxidase inhibitor (MAOI) which can prolong and intensify the cardiac stimulation and vasopressor effects of amphetamines, potentially resulting in hypertensive crisis. Methylene blue also has the potential to interact with serotonergic agents, such as amphetamines, which may increase the risk for serotonin syndrome. Serotonin syndrome is characterized by 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, gastrointestinal symptoms (e.g., nausea, vomiting, diarrhea), and in rare instances, death. Cases of serotonin syndrome have been reported, primarily following administration of standard infusions of methylene blue (1 to 8 mg/kg) as a visualizing agent in parathyroid surgery, in patients receiving selective serotonin reuptake inhibitors, serotonin/norepinephrine reuptake inhibitors, or clomipramine. It is not known if patients receiving other serotonergic psychiatric agents, such as amphetamines, with intravenous methylene blue are at a comparable risk or if methylene blue administered by other routes (e.g., orally, local injection) or in doses less than 1 mg/kg IV can produce a similar outcome. Published interaction reports between intravenously administered methylene blue and serotonergic psychiatric agents have documented symptoms including lethargy, confusion, delirium, agitation, aggression,

obtundation, myoclonus, expressive aphasia, hypertonia, pyrexia, elevated blood pressure, seizures, and/or coma. (Major) Urinary acidifying agents, such as ammonium chloride, phosphorus salts, and methenamine salts (e.g., methenamine; sodium acid phosphate), reduce the tubular reabsorption of amphetamines. As a result, amphetamine clearance is accelerated and the duration of effect is reduced. Combination therapy should be avoided if possible.
Methenamine; Sodium Salicylate: (Major) Urinary acidifying agents, such as ammonium chloride, phosphorus salts, and methenamine salts (e.g., methenamine; sodium acid phosphate), reduce the tubular reabsorption of amphetamines. As a result, amphetamine clearance is accelerated and the duration of effect is reduced. Combination therapy should be avoided if possible.
Methohexital: (Major) Inhalational general anesthetics may sensitize the myocardium to the effects of dextroamphetamine. Dosages of the amphetamines should be substantially reduced prior to surgery, and caution should be observed with concurrent use of anesthetics.
Methsuximide: (Moderate) Patients who are taking anticonvulsants for epilepsy/seizure control should use amphetamines with caution. Amphetamines may decrease the seizure threshold and may increase the risk of seizures. The amphetamines may also delay the intestinal absorption of ethosuximide; the extent of absorption of these seizure medications is not known to be affected.
Methyldopa: (Minor) Close monitoring of blood pressure or the selection of alternative therapeutic agents may be needed in patients receiving methyldopa and amphetamines. Amphetamines increase both systolic and diastolic blood pressure and may counteract the activity of some antihypertensive agents.
Methylene Blue: (Contraindicated) Amphetamines should not be administered during or within 14 days after the use of methylene blue. Methylene blue is a potent, reversible monoamine oxidase inhibitor (MAOI) which can prolong and intensify the cardiac stimulation and vasopressor effects of amphetamines, potentially resulting in hypertensive crisis. Methylene blue also has the potential to interact with serotonergic agents, such as amphetamines, which may increase the risk for serotonin syndrome. Serotonin syndrome is characterized by 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, gastrointestinal symptoms (e.g., nausea, vomiting, diarrhea), and in rare instances, death. Cases of serotonin syndrome have been reported, primarily following administration of standard infusions of methylene blue (1 to 8 mg/kg) as a visualizing agent in parathyroid surgery, in patients receiving selective serotonin reuptake inhibitors, serotonin/norepinephrine reuptake inhibitors, or clomipramine. It is not known if patients receiving other serotonergic psychiatric agents, such as

amphetamines, with intravenous methylene blue are at a comparable risk or if methylene blue administered by other routes (e.g., orally, local injection) or in doses less than 1 mg/kg IV can produce a similar outcome. Published interaction reports between intravenously administered methylene blue and serotonergic psychiatric agents have documented symptoms including lethargy, confusion, delirium, agitation, aggression, obtundation, myoclonus, expressive aphasia, hypertonia, pyrexia, elevated blood pressure, seizures, and/or coma.
Methylergonovine: (Moderate) Monitor for adverse effects if concomitant use of methylergonovine and vasoconstrictors, such as amphetamines, is necessary. Concomitant use may produce a synergistic increase in blood pressure and may also increase the risk for vasospasm which may lead to cerebral or peripheral ischemia.
metOLazone: (Minor) Amphetamines may counteract the activity of some antihypertensive agents, such as thiazide diuretics. Close monitoring of blood pressure is advised. Thiazide diuretics may also increase and prolong the actions of amphetamines by increasing the urinary pH.
Metoprolol: (Moderate) Monitor hemodynamic parameters and for loss of efficacy during concomitant sympathomimetic agent and beta-blocker use; dosage adjustments may be necessary. Concomitant use may antagonize the cardiovascular effects of either drug.
Metoprolol; hydroCHLOROthiazide, HCTZ: (Moderate) Monitor hemodynamic parameters and for loss of efficacy during concomitant sympathomimetic agent and beta-blocker use; dosage adjustments may be necessary. Concomitant use may antagonize the cardiovascular effects of either drug. (Minor) Amphetamines may counteract the activity of some antihypertensive agents, such as thiazide diuretics. Close monitoring of blood pressure is advised. Thiazide diuretics may also increase and prolong the actions of amphetamines by increasing the urinary pH.
Miglitol: (Moderate) Sympathomimetic agents and adrenergic agonists tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when pseudoephedrine, phenylephrine, and other sympathomimetics are administered to patients taking antidiabetic agents. Epinephrine and other sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.
Milnacipran: (Moderate) Coadministration of amphetamines with serotonin norepinephrine reuptake inhibitors (SNRIs) may increase the risk of serotonin syndrome. At high doses, amphetamines can increase serotonin release and act as serotonin agonists. Inform patients taking this combination of the possible increased

risk and monitor for the emergence of serotonin syndrome, particularly during treatment initiation and dose increases. If serotonin syndrome occurs, serotonergic drugs should be discontinued and appropriate medical treatment should be initiated.
Minoxidil: (Moderate) Use sympathomimetic agents with caution in patients receiving therapy for hypertension. Patients should be monitored to confirm that the desired antihypertensive effect is achieved. Sympathomimetics can increase blood pressure and heart rate, and antagonize the antihypertensive effects of vasodilators when administered concomitantly. Anginal pain may be induced when coronary insufficiency is present.
Mirtazapine: (Moderate) Coadministration of mirtazapine with amphetamines may increase the risk of serotonin syndrome. At high doses, amphetamines can increase serotonin release and act as serotonin agonists. Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome, particularly during treatment initiation and dose increases. If serotonin syndrome occurs, serotonergic drugs should be discontinued and appropriate medical treatment should be initiated.
Modafinil: (Moderate) The use of modafinil with other psychostimulants, including amphetamines (e.g., amphetamine, dextroamphetamine, lisdexamfetamine), has not been extensively studied. Patients receiving combination therapy of modafinil with other psychostimulants should be closely observed for signs of nervousness, irritability, insomnia, arrhythmias, or other CNS stimulant-related side effects. In single-dose studies of dextroamphetamine combined with modafinil, no significant pharmacokinetic interactions occurred, but a slight increase in stimulant-associated side effects was noted.
Moexipril: (Minor) Amphetamines increase both systolic and diastolic blood pressure and may counteract the activity of some antihypertensive agents, like angiotensin-converting enzyme inhibitors (ACE inhibitors). Close monitoring of blood pressure is advised.
Molindone: (Major) Concurrent use of antipsychotics and amphetamines should generally be avoided. Antipsychotics and amphetamines may interact pharmacodynamically to diminish the therapeutic effects of either agent through opposing effects on dopamine. Amphetamines are thought to block central dopamine reuptake, which has the potential to exacerbate psychosis, and antipsychotics, which are central dopamine antagonists, may diminish the effectiveness of amphetamines.
Monoamine oxidase inhibitors: (Contraindicated) In general, sympathomimetics should be avoided in patients receiving MAOIs due to an increased risk of hypertensive crisis. This applies to sympathomimetics including stimulants for ADHD, narcolepsy or weight loss, nasal, oral, and ophthalmic decongestants and cold products, and respiratory sympathomimetics (e.g., beta agonist drugs). Some local anesthetics also contain a sympathomimetic (e.g., epinephrine). In general, medicines containing

sympathomimetic agents should not be used concurrently with MAOIs or within 14 days before or after their use.
Morphine: (Moderate) If concomitant use of morphine and amphetamines is warranted, monitor patients for the emergence of serotonin syndrome. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs. The concomitant use of opioids with other drugs that affect the serotonergic neurotransmitter system has resulted in serotonin syndrome.
Nadolol: (Moderate) Monitor hemodynamic parameters and for loss of efficacy during concomitant sympathomimetic agent and beta-blocker use; dosage adjustments may be necessary. Concomitant use may antagonize the cardiovascular effects of either drug.
Nalbuphine: (Moderate) If concomitant use of nalbuphine and amphetamines is warranted, monitor patients for the emergence of serotonin syndrome. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs. The concomitant use of opioids with other drugs that affect the serotonergic neurotransmitter system has resulted in serotonin syndrome.
Naproxen; Esomeprazole: (Moderate) Use amphetamine; dextroamphetamine and proton pump inhibitors concomitantly with caution. Gastrointestinal alkalinizing agents may increase exposure to amphetamine; dextroamphetamine and exacerbate its actions.
Naratriptan: (Moderate) Monitor for signs and symptoms of serotonin syndrome, particularly during treatment initiation and dosage increase, during concomitant serotonin-receptor agonist and amphetamine; dextroamphetamine use. If serotonin syndrome occurs, discontinue therapy. Concomitant use increases the risk for serotonin syndrome.
Nateglinide: (Moderate) Sympathomimetic agents and adrenergic agonists tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when pseudoephedrine, phenylephrine, and other sympathomimetics are administered to patients taking antidiabetic agents. Epinephrine and other sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.
Nebivolol: (Moderate) Monitor hemodynamic parameters and for loss of efficacy during concomitant sympathomimetic agent and beta-blocker use; dosage adjustments may be necessary. Concomitant use may antagonize the cardiovascular effects of either drug.
Nefazodone: (Moderate) Serotonin syndrome may occur during coadministration of serotonergic drugs such as amphetamines and nefazodone. At high doses, amphetamines can increase serotonin release, as well as act as serotonin agonists.

Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome particularly after a dose increase or the addition of other serotonergic medications to an existing regimen. Discontinue all serotonergic agents if serotonin syndrome occurs and implement appropriate medical management.
NiCARdipine: (Minor) Amphetamines increase both systolic and diastolic blood pressure and may counteract the activity of some antihypertensive agents, like calcium-channel blockers. Close monitoring of blood pressure is advised.
NIFEdipine: (Minor) Amphetamines increase both systolic and diastolic blood pressure and may counteract the activity of some antihypertensive agents, like calcium-channel blockers. Close monitoring of blood pressure is advised.
niMODipine: (Minor) Amphetamines increase both systolic and diastolic blood pressure and may counteract the activity of some antihypertensive agents, like calcium-channel blockers. Close monitoring of blood pressure is advised.
Nirmatrelvir; Ritonavir: (Moderate) Warn patients that the risk of amphetamine toxicity may be increased during concurrent use of ritonavir, a strong CYP2D6 inhibitor. Amphetamines are partially metabolized by CYP2D6 and have serotonergic properties; inhibition of amphetamine metabolism may increase the risk of serotonin syndrome or other toxicity. If serotonin syndrome occurs, both the amphetamine and CYP2D6 inhibitor should be discontinued and appropriate medical treatment should be implemented.
Nisoldipine: (Minor) Amphetamines increase both systolic and diastolic blood pressure and may counteract the activity of some antihypertensive agents, like calcium-channel blockers. Close monitoring of blood pressure is advised.
Nitrates: (Moderate) Sympathomimetics can antagonize the antianginal effects of nitrates, and can increase blood pressure and/or heart rate. Anginal pain may be induced when coronary insufficiency is present.
Nitroglycerin: (Moderate) Sympathomimetics can antagonize the antianginal effects of nitrates, and can increase blood pressure and/or heart rate. Anginal pain may be induced when coronary insufficiency is present.
Nitroprusside: (Moderate) Use sympathomimetic agents with caution in patients receiving therapy for hypertension. Patients should be monitored to confirm that the desired antihypertensive effect is achieved. Sympathomimetics can increase blood pressure and heart rate, and antagonize the antihypertensive effects of vasodilators when administered concomitantly. Anginal pain may be induced when coronary insufficiency is present.
Nizatidine: (Moderate) Use amphetamine; dextroamphetamine and H2-blockers concomitantly with caution. Gastrointestinal alkalinizing agents may increase exposure to amphetamine; dextroamphetamine and exacerbate its actions.
Non-Ionic Contrast Media: (Major) Use of medications that lower the seizure threshold should be carefully evaluated when considering the use of intrathecal radiopaque

contrast agents. Amphetamines should be discontinued at least 48 hours before myelography and should not be resumed for at least 24 hours postprocedure.
Nortriptyline: (Moderate) Monitor blood pressure, heart rate, and for signs and symptoms of serotonin syndrome, particularly during treatment initiation and dosage increase, during concomitant amphetamine and tricyclic antidepressant use. Adjust doses or use alternative therapy based on clinical response. If serotonin syndrome occurs, discontinue therapy. Concomitant use increases the risk for potentiation of cardiovascular effects and serotonin syndrome. Amphetamines may enhance the activity of tricyclic antidepressants causing significant and sustained increases in amphetamine concentrations in the brain.
OLANZapine; FLUoxetine: (Moderate) Monitor for signs and symptoms of serotonin syndrome, particularly during treatment initiation and dosage increase, during concomitant amphetamine and fluoxetine use. If serotonin syndrome occurs, discontinue therapy. Concomitant use increases the risk for serotonin syndrome.
Oliceridine: (Moderate) If concomitant use of oliceridine and amphetamines is warranted, monitor patients for the emergence of serotonin syndrome. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs. The concomitant use of opioids with other drugs that affect the serotonergic neurotransmitter system has resulted in serotonin syndrome.
Olmesartan: (Minor) Amphetamines increase both systolic and diastolic blood pressure and may counteract the activity of some antihypertensive agents, such as angiotensin II receptor antagonists. Close monitoring of blood pressure is advised.
Olmesartan; amLODIPine; hydroCHLOROthiazide, HCTZ: (Minor) Amphetamines increase both systolic and diastolic blood pressure and may counteract the activity of some antihypertensive agents, like calcium-channel blockers. Close monitoring of blood pressure is advised. (Minor) Amphetamines increase both systolic and diastolic blood pressure and may counteract the activity of some antihypertensive agents, such as angiotensin II receptor antagonists. Close monitoring of blood pressure is advised. (Minor) Amphetamines may counteract the activity of some antihypertensive agents, such as thiazide diuretics. Close monitoring of blood pressure is advised. Thiazide diuretics may also increase and prolong the actions of amphetamines by increasing the urinary pH.
Olmesartan; hydroCHLOROthiazide, HCTZ: (Minor) Amphetamines increase both systolic and diastolic blood pressure and may counteract the activity of some antihypertensive agents, such as angiotensin II receptor antagonists. Close monitoring of blood pressure is advised. (Minor) Amphetamines may counteract the activity of some antihypertensive agents, such as thiazide diuretics. Close monitoring of blood pressure is advised. Thiazide diuretics may also increase and prolong the actions of amphetamines by increasing the urinary pH.
Omeprazole: (Moderate) Use amphetamine; dextroamphetamine and proton pump

inhibitors concomitantly with caution. Gastrointestinal alkalinizing agents may increase exposure to amphetamine; dextroamphetamine and exacerbate its actions.
Omeprazole; Amoxicillin; Rifabutin: (Moderate) Use amphetamine; dextroamphetamine and proton pump inhibitors concomitantly with caution. Gastrointestinal alkalinizing agents may increase exposure to amphetamine; dextroamphetamine and exacerbate its actions.
Omeprazole; Sodium Bicarbonate: (Moderate) Monitor for an increase in the incidence and severity of amphetamine-related adverse effects during concomitant use of urinary alkalinizing agents. Increasing urine pH may increase amphetamine exposure by reducing urinary excretion of amphetamine. A urine pH more than 7.5 has been observed to increase the half-life of amphetamine from 8 to 10.5 hours to 16 to 31 hours when compared to a pH less than 6. Additionally, a urine pH more than 8 has been observed to reduce the amount of amphetamine excreted in the urine over 16 hours to less than 3% of the original dose; a 5-fold reduction compared to controls.
(Moderate) Use amphetamine; dextroamphetamine and proton pump inhibitors concomitantly with caution. Gastrointestinal alkalinizing agents may increase exposure to amphetamine; dextroamphetamine and exacerbate its actions.
oxyCODONE: (Moderate) If concomitant use of oxycodone and amphetamines is warranted, monitor patients for the emergence of serotonin syndrome. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs. The concomitant use of opioids with other drugs that affect the serotonergic neurotransmitter system has resulted in serotonin syndrome.
oxyMORphone: (Moderate) If concomitant use of oxymorphone and amphetamines is warranted, monitor patients for the emergence of serotonin syndrome. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs. The concomitant use of opioids with other drugs that affect the serotonergic neurotransmitter system has resulted in serotonin syndrome.
Pantoprazole: (Moderate) Use amphetamine; dextroamphetamine and proton pump inhibitors concomitantly with caution. Gastrointestinal alkalinizing agents may increase exposure to amphetamine; dextroamphetamine and exacerbate its actions.
PARoxetine: (Moderate) Monitor for signs and symptoms of serotonin syndrome, particularly during treatment initiation and dosage increase, during concomitant amphetamine and paroxetine use. If serotonin syndrome occurs, discontinue therapy. Concomitant use increases the risk for serotonin syndrome.
Perindopril: (Minor) Amphetamines increase both systolic and diastolic blood pressure and may counteract the activity of some antihypertensive agents, like angiotensin-converting enzyme inhibitors (ACE inhibitors). Close monitoring of blood pressure is advised.
Perindopril; amLODIPine: (Minor) Amphetamines increase both systolic and diastolic blood pressure and may counteract the activity of some antihypertensive agents, like

angiotensin-converting enzyme inhibitors (ACE inhibitors). Close monitoring of blood pressure is advised. (Minor) Amphetamines increase both systolic and diastolic blood pressure and may counteract the activity of some antihypertensive agents, like calcium-channel blockers. Close monitoring of blood pressure is advised.
Perphenazine; Amitriptyline: (Moderate) Monitor blood pressure, heart rate, and for signs and symptoms of serotonin syndrome, particularly during treatment initiation and dosage increase, during concomitant amphetamine and tricyclic antidepressant use. Adjust doses or use alternative therapy based on clinical response. If serotonin syndrome occurs, discontinue therapy. Concomitant use increases the risk for potentiation of cardiovascular effects and serotonin syndrome. Amphetamines may enhance the activity of tricyclic antidepressants causing significant and sustained increases in amphetamine concentrations in the brain.
Phenelzine: (Contraindicated) In general, sympathomimetics should be avoided in patients receiving MAOIs due to an increased risk of hypertensive crisis. This applies to sympathomimetics including stimulants for ADHD, narcolepsy or weight loss, nasal, oral, and ophthalmic decongestants and cold products, and respiratory sympathomimetics (e.g., beta agonist drugs). Some local anesthetics also contain a sympathomimetic (e.g., epinephrine). In general, medicines containing sympathomimetic agents should not be used concurrently with MAOIs or within 14 days before or after their use.
PHENobarbital: (Major) Patients who are taking anticonvulsants for epilepsy/seizure control should use dextroamphetamine with caution. Amphetamines may decrease the seizure threshold and may increase the risk of seizures. If seizures occur, amphetamine discontinuation may be necessary. Additionally, the amphetamines may delay the intestinal absorption of phenobarbital; the extent of absorption of these seizure medications is not known to be affected.
PHENobarbital; Hyoscyamine; Atropine; Scopolamine: (Major) Patients who are taking anticonvulsants for epilepsy/seizure control should use dextroamphetamine with caution. Amphetamines may decrease the seizure threshold and may increase the risk of seizures. If seizures occur, amphetamine discontinuation may be necessary. Additionally, the amphetamines may delay the intestinal absorption of phenobarbital; the extent of absorption of these seizure medications is not known to be affected.
Phenoxybenzamine: (Major) Amphetamines increase both systolic and diastolic blood pressure and may counteract the activity of some antihypertensive agents. Due to the risk of unopposed alpha-adrenergic activity, amphetamines should be used cautiously with beta-blockers. Increased blood pressure, bradycardia, or heart block may occur due to excessive alpha-adrenergic receptor stimulation. In particular, amphetamines can inhibit the antihypertensive response to guanadrel, an adrenergic antagonist that causes depletion of norepinephrine in the synapse. Close monitoring of blood pressure or the selection of alternative therapeutic agents may be needed.
Phentermine: (Major) Avoid coadministration of phentermine and other medications for

weight loss, such as amphetamines. The safety and efficacy of combination therapy have not been established.
Phentermine; Topiramate: (Major) Avoid coadministration of phentermine and other medications for weight loss, such as amphetamines. The safety and efficacy of combination therapy have not been established. (Moderate) Monitor for amphetamine-related adverse events if coadministered with topiramate. Concurrent use may increase amphetamine concentrations, resulting in potentiation of the action of amphetamines.
Phentolamine: (Major) Amphetamines increase both systolic and diastolic blood pressure and may counteract the activity of some antihypertensive agents. Due to the risk of unopposed alpha-adrenergic activity, amphetamines should be used cautiously with beta-blockers. Increased blood pressure, bradycardia, or heart block may occur due to excessive alpha-adrenergic receptor stimulation. Phentolamine may decrease, but not completely reverse, the pressor response of amphetamine overdose. Close monitoring of blood pressure or the selection of alternative therapeutic agents may be needed.
Phenytoin: (Moderate) Monitor for decreased efficacy of phenytoin during coadministration with amphetamine; dextroamphetamine salts. Amphetamines may delay the intestinal absorption of phenytoin.
Pindolol: (Moderate) Monitor hemodynamic parameters and for loss of efficacy during concomitant sympathomimetic agent and beta-blocker use; dosage adjustments may be necessary. Concomitant use may antagonize the cardiovascular effects of either drug.
Pioglitazone: (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking thiazolidinediones. Sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.
Pioglitazone; Glimepiride: (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking sulfonylureas. Sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes. (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking thiazolidinediones.

Sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.
Pioglitazone; metFORMIN: (Moderate) Monitor for loss of glycemic control when amphetamines are administered to patients taking antidiabetic agents. Sympathomimetic agents and adrenergic agonists tend to increase blood glucose concentrations when administered systemically. Sympathomimetic agents, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking thiazolidinediones. Sympathomimetics, through stimulation of alpha- and beta-receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.
Potassium Bicarbonate: (Moderate) Monitor for an increase in the incidence and severity of amphetamine-related adverse effects during concomitant use of urinary alkalinizing agents. Increasing urine pH may increase amphetamine exposure by reducing urinary excretion of amphetamine. A urine pH more than 7.5 has been observed to increase the half-life of amphetamine from 8 to 10.5 hours to 16 to 31 hours when compared to a pH less than 6. Additionally, a urine pH more than 8 has been observed to reduce the amount of amphetamine excreted in the urine over 16 hours to less than 3% of the original dose; a 5-fold reduction compared to controls.
Potassium Citrate: (Moderate) Monitor for an increase in the incidence and severity of amphetamine-related adverse effects during concomitant use of urinary alkalinizing agents. Increasing urine pH may increase amphetamine exposure by reducing urinary excretion of amphetamine. A urine pH more than 7.5 has been observed to increase the half-life of amphetamine from 8 to 10.5 hours to 16 to 31 hours when compared to a pH less than 6. Additionally, a urine pH more than 8 has been observed to reduce the amount of amphetamine excreted in the urine over 16 hours to less than 3% of the original dose; a 5-fold reduction compared to controls.
Potassium Citrate; Citric Acid: (Moderate) Monitor for an increase in the incidence and severity of amphetamine-related adverse effects during concomitant use of urinary alkalinizing agents. Increasing urine pH may increase amphetamine exposure by

reducing urinary excretion of amphetamine. A urine pH more than 7.5 has been observed to increase the half-life of amphetamine from 8 to 10.5 hours to 16 to 31 hours when compared to a pH less than 6. Additionally, a urine pH more than 8 has been observed to reduce the amount of amphetamine excreted in the urine over 16 hours to less than 3% of the original dose; a 5-fold reduction compared to controls.
Potassium-sparing diuretics: (Minor) Amphetamines increase both systolic and diastolic blood pressure and may counteract the activity of some antihypertensive agents, like potassium-sparing diuretics. Close monitoring of blood pressure is advised.
Pramlintide: (Moderate) Sympathomimetic agents and adrenergic agonists tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when pseudoephedrine, phenylephrine, and other sympathomimetics are administered to patients taking antidiabetic agents. Epinephrine and other sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.
Prazosin: (Minor) Close monitoring of blood pressure or the selection of alternative therapeutic agents may be needed in patients receiving prazosin and amphetamines. Amphetamines increase both systolic and diastolic blood pressure and may counteract the activity of some antihypertensive agents, such as prazosin.
Prilocaine; EPINEPHrine: (Moderate) Monitor blood pressure and heart rate during concomitant amphetamine and epinephrine use. Amphetamines may potentiate the pressor effects of epinephrine.
Primidone: (Major) Patients who are taking anticonvulsants for epilepsy/seizure control should use amphetamines with caution. Amphetamines may decrease the seizure threshold and may increase the risk of seizures.
Procarbazine: (Major) Because procarbazine exhibits some monoamine oxidase inhibitory (MAOI) activity, sympathomimetic drugs should be avoided. As with MAOIs, the use of a sympathomimetic drug with procarbazine may precipitate hypertensive crisis or other serious side effects. In the presence of MAOIs, drugs that cause release of norepinephrine induce severe cardiovascular and cerebrovascular responses. In general, do not use a sympathomimetic drug unless clinically necessary (e.g., medical emergencies, agents like dopamine) within the 14 days prior, during or 14 days after procarbazine therapy. If use is necessary within 2 weeks of the MAOI drug, in general the initial dose of the sympathomimetic agent must be greatly reduced. Patients should be counseled to avoid non-prescription (OTC) decongestants and other drug products, weight loss products, and energy supplements that contain sympathomimetic agents.
Propofol: (Major) Inhalational general anesthetics may sensitize the myocardium to the

effects of dextroamphetamine. Dosages of the amphetamines should be substantially reduced prior to surgery, and caution should be observed with concurrent use of anesthetics.
Propranolol: (Moderate) Monitor hemodynamic parameters and for loss of efficacy during concomitant sympathomimetic agent and beta-blocker use; dosage adjustments may be necessary. Concomitant use may antagonize the cardiovascular effects of either drug.
Proton pump inhibitors: (Moderate) Use amphetamine; dextroamphetamine and proton pump inhibitors concomitantly with caution. Gastrointestinal alkalinizing agents may increase exposure to amphetamine; dextroamphetamine and exacerbate its actions.
Protriptyline: (Moderate) Monitor blood pressure, heart rate, and for signs and symptoms of serotonin syndrome, particularly during treatment initiation and dosage increase, during concomitant amphetamine and tricyclic antidepressant use. Adjust doses or use alternative therapy based on clinical response. If serotonin syndrome occurs, discontinue therapy. Concomitant use increases the risk for potentiation of cardiovascular effects and serotonin syndrome. Amphetamines may enhance the activity of tricyclic antidepressants causing significant and sustained increases in amphetamine concentrations in the brain.
Pseudoephedrine; Triprolidine: (Moderate) Amphetamines may pharmacodynamically counteract the sedative properties of some antihistamines, such as the sedating H1-blockers (i.e., diphenhydramine). This effect may be clinically important if a patient is receiving an antihistamine agent for treatment of insomnia. Alternatively, if a patient is receiving an amphetamine for treatment of narcolepsy, the combination with a sedating antihistamine may reverse the action of the amphetamine.
Quinapril: (Minor) Amphetamines increase both systolic and diastolic blood pressure and may counteract the activity of some antihypertensive agents, like angiotensin-converting enzyme inhibitors (ACE inhibitors). Close monitoring of blood pressure is advised.
Quinapril; hydroCHLOROthiazide, HCTZ: (Minor) Amphetamines increase both systolic and diastolic blood pressure and may counteract the activity of some antihypertensive agents, like angiotensin-converting enzyme inhibitors (ACE inhibitors). Close monitoring of blood pressure is advised. (Minor) Amphetamines may counteract the activity of some antihypertensive agents, such as thiazide diuretics. Close monitoring of blood pressure is advised. Thiazide diuretics may also increase and prolong the actions of amphetamines by increasing the urinary pH.
quiNIDine: (Moderate) Warn patients that the risk of amphetamine toxicity may be increased during concurrent use of quinidine, a strong CYP2D6 inhibitor. Amphetamines are partially metabolized by CYP2D6 and have serotonergic properties; inhibition of amphetamine metabolism may increase the risk of serotonin syndrome or other toxicity. If serotonin syndrome occurs, both the amphetamine and CYP2D6 inhibitor

should be discontinued and appropriate medical treatment should be implemented.
RABEprazole: (Moderate) Use amphetamine; dextroamphetamine and proton pump inhibitors concomitantly with caution. Gastrointestinal alkalinizing agents may increase exposure to amphetamine; dextroamphetamine and exacerbate its actions.
Racepinephrine: (Major) Racepinephrine is a sympathomimetic drug with agonist actions at both the alpha and beta receptors. Patients using racepinephrine inhalation are advised to avoid other non-prescription products containing sympathomimetics since additive adverse effects on the cardiovascular and nervous system are possible, some which may be undesirable. Side effects such as nausea, tremor, nervousness, difficulty with sleep, and increased heart rate or blood pressure may be additive. Patients should avoid use of non-prescription decongestants, such as phenylephrine and pseudoephedrine, while using racepinephrine inhalations. Patients should avoid dietary supplements containing ingredients that are reported or claimed to have a stimulant or weight-loss effect, such as ephedrine and ephedra, Ma huang, and phenylpropanolamine. Patients taking prescription sympathomimetic or stimulant medications (including amphetamines, methylphenidate, dexmethylphenidate, isometheptane, epinephrine) should seek health care professional advice prior to the use of racepinephrine inhalations; consider therapeutic alternatives to racepinephrine for these patients.
Ramipril: (Minor) Amphetamines increase both systolic and diastolic blood pressure and may counteract the activity of some antihypertensive agents, like angiotensin-converting enzyme inhibitors (ACE inhibitors). Close monitoring of blood pressure is advised.
Rasagiline: (Moderate) The concomitant use of rasagiline and sympathomimetics was not allowed in clinical studies; therefore, caution is advised during concurrent use of rasagiline and sympathomimetics including stimulants for ADHD and weight loss, non-prescription nasal, oral, and ophthalmic decongestants, and weight loss dietary supplements containing Ephedra. Although sympathomimetics are contraindicated for use with other non-selective monoamine oxidase inhibitors (MAOIs), hypertensive reactions generally are not expected to occur during concurrent use with rasagiline because of the selective monoamine oxidase-B (MAO-B) inhibition of rasagiline at manufacturer recommended doses. One case of elevated blood pressure has been reported in a patient during concurrent use of the recommended dose of rasagiline and ophthalmic tetrahydrozoline. One case of hypertensive crisis has been reported in a patient taking the recommended dose of another MAO-B inhibitor, selegiline, in combination with ephedrine. It should be noted that the MAO-B selectivity of rasagiline decreases in a dose-related manner as increases are made above the recommended daily dose and interactions with sympathomimetics may be more likely to occur at these higher doses.
Regular Insulin: (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control

when sympathomimetics are administered to patients taking insulin. Sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.
Regular Insulin; Isophane Insulin (NPH): (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking insulin. Sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.
Remifentanil: (Moderate) Because of the potential risk and severity of serotonin syndrome, caution should be observed when administering remifentanil with amphetamines. Inform patients taking this combination of the possible increased risks and monitor for the emergence of serotonin syndrome particularly during treatment initiation and dose adjustment. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs.
Repaglinide: (Moderate) Sympathomimetic agents and adrenergic agonists tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when pseudoephedrine, phenylephrine, and other sympathomimetics are administered to patients taking antidiabetic agents. Epinephrine and other sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.
Riociguat: (Major) Avoid use of sympathomimetic agents with riociguat. Sympathomimetics counteract the medications used to stabilize pulmonary hypertension, including riociguat. Sympathomimetics can increase blood pressure, increase heart rate, and may cause vasoconstriction resulting in chest pain and shortness of breath in these patients. Patients should be advised to avoid amphetamine drugs, decongestants (including nasal decongestants) and sympathomimetic anorexiants for weight loss, including dietary supplements. Intravenous vasopressors may be used in the emergency management of pulmonary hypertension patients when

needed, but hemodynamic monitoring and careful monitoring of cardiac status are needed to avoid ischemia and other complications.
Ritonavir: (Moderate) Warn patients that the risk of amphetamine toxicity may be increased during concurrent use of ritonavir, a strong CYP2D6 inhibitor. Amphetamines are partially metabolized by CYP2D6 and have serotonergic properties; inhibition of amphetamine metabolism may increase the risk of serotonin syndrome or other toxicity. If serotonin syndrome occurs, both the amphetamine and CYP2D6 inhibitor should be discontinued and appropriate medical treatment should be implemented.
Rizatriptan: (Moderate) Monitor for signs and symptoms of serotonin syndrome, particularly during treatment initiation and dosage increase, during concomitant serotonin-receptor agonist and amphetamine; dextroamphetamine use. If serotonin syndrome occurs, discontinue therapy. Concomitant use increases the risk for serotonin syndrome.
Rosiglitazone: (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking thiazolidinediones. Sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.
Sacubitril; Valsartan: (Minor) Amphetamines increase both systolic and diastolic blood pressure and may counteract the activity of some antihypertensive agents, such as angiotensin II receptor antagonists. Close monitoring of blood pressure is advised.
Safinamide: (Contraindicated) Safinamide, a selective monoamine oxidase-B inhibitor, is contraindicated for use with amphetamines due to the risk of serotonin syndrome or hypertensive crisis. The manufacturer of safinamide recommends that a period of at least 14 days elapse between the discontinuation of safinamide and the initiation of serotonergic agents. Hypertensive crisis has been reported in patients taking recommended doses of selective MAO-B inhibitors and sympathomimetic medications, such as amphetamines. Safinamide can cause hypertension or exacerbate existing hypertension, particularly at daily dosages exceeding those recommended by the manufacturer.
Salmeterol: (Moderate) Monitor blood pressure and heart rate during concomitant amphetamine; dextroamphetamine and salmeterol use. Concomitant use may potentiate sympathetic effects.
sAXagliptin: (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking dipeptidyl peptidase-4

(DPP-4) inhibitors. Sympathomimetics, through stimulation of alpha- and beta-receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.
Sedating H1-blockers: (Moderate) Amphetamines may pharmacodynamically counteract the sedative properties of some antihistamines, such as the sedating H1-blockers (i.e., diphenhydramine). This effect may be clinically important if a patient is receiving an antihistamine agent for treatment of insomnia. Alternatively, if a patient is receiving an amphetamine for treatment of narcolepsy, the combination with a sedating antihistamine may reverse the action of the amphetamine.
Selegiline: (Contraindicated) The product labels for amphetamines contraindicate use with monoamine oxidase inhibitors (MAOIs), including selegiline, due to the risk of hypertensive crisis or serotonin syndrome. Amphetamines should not be used concurrently with MAOIs or within 14 days before or after their use. The manufacturers of selegiline products recommend caution and monitoring of blood pressure during concurrent use with sympathomimetics.
Selexipag: (Major) Avoid use of sympathomimetic agents with selexipag. Sympathomimetics counteract the medications used to stabilize pulmonary hypertension, including selexipag. Sympathomimetics can increase blood pressure, increase heart rate, and may cause vasoconstriction resulting in chest pain and shortness of breath in these patients. Patients should be advised to avoid amphetamine drugs, decongestants (including nasal decongestants) and sympathomimetic anorexiants for weight loss, including dietary supplements. Intravenous vasopressors may be used in the emergency management of pulmonary hypertension patients when needed, but hemodynamic monitoring and careful monitoring of cardiac status are needed to avoid ischemia and other complications.
Semaglutide: (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking incretin mimetics. Sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.
Serotonin norepinephrine reuptake inhibitors: (Moderate) Coadministration of amphetamines with serotonin norepinephrine reuptake inhibitors (SNRIs) may increase the risk of serotonin syndrome. At high doses, amphetamines can increase serotonin

release and act as serotonin agonists. Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome, particularly during treatment initiation and dose increases. If serotonin syndrome occurs, serotonergic drugs should be discontinued and appropriate medical treatment should be initiated.
Serotonin-Receptor Agonists: (Moderate) Monitor for signs and symptoms of serotonin syndrome, particularly during treatment initiation and dosage increase, during concomitant serotonin-receptor agonist and amphetamine; dextroamphetamine use. If serotonin syndrome occurs, discontinue therapy. Concomitant use increases the risk for serotonin syndrome.
Sertraline: (Moderate) Coadministration of selective serotonin reuptake inhibitors (SSRIs) like sertraline with amphetamines may increase the risk of serotonin syndrome. At high doses, amphetamines can increase serotonin release and act as serotonin agonists. Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome, particularly during treatment initiation and dose increases. If serotonin syndrome occurs, serotonergic drugs should be discontinued and appropriate medical treatment should be initiated.
Sevoflurane: (Major) Inhalational general anesthetics (e.g., enflurane, halothane, isoflurane, and methoxyflurane) may sensitize the myocardium to the effects of stimulants. Dosages of the amphetamines should be substantially reduced prior to surgery, and caution should be observed with concurrent use of anesthetics.
SGLT2 Inhibitors: (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking SGLT2 inhibitors. Sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.
SITagliptin: (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking dipeptidyl peptidase-4 (DPP-4) inhibitors. Sympathomimetics, through stimulation of alpha- and beta-receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.
Sodium Acetate: (Moderate) Monitor for an increase in the incidence and severity of

amphetamine-related adverse effects during concomitant use of urinary alkalinizing agents. Increasing urine pH may increase amphetamine exposure by reducing urinary excretion of amphetamine. A urine pH more than 7.5 has been observed to increase the half-life of amphetamine from 8 to 10.5 hours to 16 to 31 hours when compared to a pH less than 6. Additionally, a urine pH more than 8 has been observed to reduce the amount of amphetamine excreted in the urine over 16 hours to less than 3% of the original dose; a 5-fold reduction compared to controls.
Sodium Bicarbonate: (Moderate) Monitor for an increase in the incidence and severity of amphetamine-related adverse effects during concomitant use of urinary alkalinizing agents. Increasing urine pH may increase amphetamine exposure by reducing urinary excretion of amphetamine. A urine pH more than 7.5 has been observed to increase the half-life of amphetamine from 8 to 10.5 hours to 16 to 31 hours when compared to a pH less than 6. Additionally, a urine pH more than 8 has been observed to reduce the amount of amphetamine excreted in the urine over 16 hours to less than 3% of the original dose; a 5-fold reduction compared to controls.
Sodium Citrate; Citric Acid: (Moderate) Monitor for an increase in the incidence and severity of amphetamine-related adverse effects during concomitant use of urinary alkalinizing agents. Increasing urine pH may increase amphetamine exposure by reducing urinary excretion of amphetamine. A urine pH more than 7.5 has been observed to increase the half-life of amphetamine from 8 to 10.5 hours to 16 to 31 hours when compared to a pH less than 6. Additionally, a urine pH more than 8 has been observed to reduce the amount of amphetamine excreted in the urine over 16 hours to less than 3% of the original dose; a 5-fold reduction compared to controls.
Sodium Lactate: (Moderate) Monitor for an increase in the incidence and severity of amphetamine-related adverse effects during concomitant use of urinary alkalinizing agents. Increasing urine pH may increase amphetamine exposure by reducing urinary excretion of amphetamine. A urine pH more than 7.5 has been observed to increase the half-life of amphetamine from 8 to 10.5 hours to 16 to 31 hours when compared to a pH less than 6. Additionally, a urine pH more than 8 has been observed to reduce the amount of amphetamine excreted in the urine over 16 hours to less than 3% of the original dose; a 5-fold reduction compared to controls.
Sodium Oxybate: (Moderate) Sodium oxybate has the potential to induce seizures; it has been speculated that this effect may be mediated through the action of sodium oxybate at GABA receptors. Although convulsant effects occur primarily at high dosages, sodium oxybate should be used cautiously with psychostimulants that are known to lower seizure threshold such as the amphetamines. Note that CNS stimulants, including the amphetamines, are frequently used in the treatment of narcolepsy, and clinical trials involving the use of psychostimulants with sodium oxybate have not found the combinations to be unsafe. Pharmacodynamic interactions cannot be ruled out, however.

Solriamfetol: (Moderate) Monitor blood pressure and heart rate during coadministration of solriamfetol, a norepinephrine and dopamine reuptake inhibitor, and amphetamines, which are CNS stimulants. Concurrent use of solriamfetol and other medications that increase blood pressure and/or heart rate may increase the risk of such effects. Coadministration of solriamfetol with other drugs that increase blood pressure or heart rate has not been evaluated.
Sotagliflozin: (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking SGLT2 inhibitors. Sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.
Sotalol: (Moderate) Monitor hemodynamic parameters and for loss of efficacy during concomitant sympathomimetic agent and beta-blocker use; dosage adjustments may be necessary. Concomitant use may antagonize the cardiovascular effects of either drug.
Spironolactone: (Minor) Amphetamines increase both systolic and diastolic blood pressure and may counteract the activity of some antihypertensive agents, like potassium-sparing diuretics. Close monitoring of blood pressure is advised.
Spironolactone; hydroCHLOROthiazide, HCTZ: (Minor) Amphetamines increase both systolic and diastolic blood pressure and may counteract the activity of some antihypertensive agents, like potassium-sparing diuretics. Close monitoring of blood pressure is advised. (Minor) Amphetamines may counteract the activity of some antihypertensive agents, such as thiazide diuretics. Close monitoring of blood pressure is advised. Thiazide diuretics may also increase and prolong the actions of amphetamines by increasing the urinary pH.
St. John's Wort, Hypericum perforatum: (Moderate) Coadministration of St. John's Wort with amphetamines may increase the risk of serotonin syndrome. Serotonin syndrome has been reported with both drugs when taken alone, but especially when coadministered with other serotonergic agents. Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome. Discontinue serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs.
Succinimides: (Moderate) Patients who are taking anticonvulsants for epilepsy/seizure control should use amphetamines with caution. Amphetamines may decrease the seizure threshold and may increase the risk of seizures. The amphetamines may also delay the intestinal absorption of ethosuximide; the extent of absorption of these seizure medications is not known to be affected.

SUFentanil: (Moderate) Because of the potential risk and severity of serotonin syndrome, caution should be observed when administering sufentanil with amphetamines. Inform patients taking this combination of the possible increased risks and monitor for the emergence of serotonin syndrome particularly during treatment initiation and dose adjustment. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs.
Sulfacetamide; Sulfur: (Moderate) Monitor for an increase in the incidence and severity of amphetamine-related adverse effects during concomitant use of urinary alkalinizing agents. Increasing urine pH may increase amphetamine exposure by reducing urinary excretion of amphetamine. A urine pH more than 7.5 has been observed to increase the half-life of amphetamine from 8 to 10.5 hours to 16 to 31 hours when compared to a pH less than 6. Additionally, a urine pH more than 8 has been observed to reduce the amount of amphetamine excreted in the urine over 16 hours to less than 3% of the original dose; a 5-fold reduction compared to controls.
Sulfonylureas: (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking sulfonylureas. Sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.
SUMAtriptan: (Moderate) Monitor for signs and symptoms of serotonin syndrome, particularly during treatment initiation and dosage increase, during concomitant serotonin-receptor agonist and amphetamine; dextroamphetamine use. If serotonin syndrome occurs, discontinue therapy. Concomitant use increases the risk for serotonin syndrome.
SUMAtriptan; Naproxen: (Moderate) Monitor for signs and symptoms of serotonin syndrome, particularly during treatment initiation and dosage increase, during concomitant serotonin-receptor agonist and amphetamine; dextroamphetamine use. If serotonin syndrome occurs, discontinue therapy. Concomitant use increases the risk for serotonin syndrome.
Tapentadol: (Moderate) If concomitant use of tapentadol and amphetamines is warranted, monitor patients for the emergence of serotonin syndrome. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs. The concomitant use of opioids with other drugs that affect the serotonergic neurotransmitter system has resulted in serotonin syndrome.
Telmisartan: (Minor) Amphetamines increase both systolic and diastolic blood pressure and may counteract the activity of some antihypertensive agents, such as angiotensin II

receptor antagonists. Close monitoring of blood pressure is advised.
Telmisartan; amLODIPine: (Minor) Amphetamines increase both systolic and diastolic blood pressure and may counteract the activity of some antihypertensive agents, like calcium-channel blockers. Close monitoring of blood pressure is advised. (Minor) Amphetamines increase both systolic and diastolic blood pressure and may counteract the activity of some antihypertensive agents, such as angiotensin II receptor antagonists. Close monitoring of blood pressure is advised.
Telmisartan; hydroCHLOROthiazide, HCTZ: (Minor) Amphetamines increase both systolic and diastolic blood pressure and may counteract the activity of some antihypertensive agents, such as angiotensin II receptor antagonists. Close monitoring of blood pressure is advised. (Minor) Amphetamines may counteract the activity of some antihypertensive agents, such as thiazide diuretics. Close monitoring of blood pressure is advised. Thiazide diuretics may also increase and prolong the actions of amphetamines by increasing the urinary pH.
Terazosin: (Minor) Close monitoring of blood pressure or the selection of alternative therapeutic agents may be needed in patients receiving terazosin and amphetamines. Amphetamines increase both systolic and diastolic blood pressure and may counteract the activity of some antihypertensive agents, such as terazosin.
Terbutaline: (Major) Concomitant use of sympathomimetics with beta-agonists might result in additive cardiovascular effects such as increased blood pressure and heart rate.
Theophylline, Aminophylline: (Moderate) Concurrent administration of theophylline or aminophylline with some sympathomimetics can produce excessive stimulation and effects such as nervousness, irritability, or insomnia. Seizures or cardiac arrhythmias are also possible. (Moderate) Concurrent administration of theophylline or aminophylline with sympathomimetics can produce excessive stimulation manifested by skeletal muscle activity, agitation, and hyperactivity.
Thiazide diuretics: (Minor) Amphetamines may counteract the activity of some antihypertensive agents, such as thiazide diuretics. Close monitoring of blood pressure is advised. Thiazide diuretics may also increase and prolong the actions of amphetamines by increasing the urinary pH.
Thiazolidinediones: (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking thiazolidinediones. Sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.
Thiothixene: (Major) Concurrent use of antipsychotics, such as thiothixene, and

amphetamines should generally be avoided. Antipsychotics and amphetamines may interact pharmacodynamically to diminish the therapeutic effects of either agent through opposing effects on dopamine. Amphetamines are thought to block central dopamine reuptake, which has the potential to exacerbate psychosis, and antipsychotics, which are central dopamine antagonists, may diminish the effectiveness of amphetamines.
Thyroid hormones: (Moderate) Monitor hemodynamic parameters during concomitant sympathomimetic agent and thyroid hormone use; dosage adjustments may be necessary. Concomitant use may increase the effects of sympathomimetics or thyroid hormone.
Timolol: (Moderate) Monitor hemodynamic parameters and for loss of efficacy during concomitant sympathomimetic agent and beta-blocker use; dosage adjustments may be necessary. Concomitant use may antagonize the cardiovascular effects of either drug.
Tipranavir: (Moderate) Warn patients that there are potentially serious drug interactions between tipranavir and prescription amphetamine therapy or illicit amphetamine use. The risk of amphetamine toxicity may be increased during concurrent use of potent CYP2D6 inhibitors such as tipranavir. Amphetamines are partially metabolized by CYP2D6 and have serotonergic properties; inhibition of amphetamine metabolism may increase the risk of serotonin syndrome or other toxicity. If serotonin syndrome occurs, discontinue both the amphetamine and CYP2D6 inhibitor and initiate appropriate medical treatment.
Tirzepatide: (Moderate) Sympathomimetic agents tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when sympathomimetics are administered to patients taking incretin mimetics. Sympathomimetics, through stimulation of alpha- and beta- receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.
Topiramate: (Moderate) Monitor for amphetamine-related adverse events if coadministered with topiramate. Concurrent use may increase amphetamine concentrations, resulting in potentiation of the action of amphetamines.
Torsemide: (Minor) Amphetamine and Dextroamphetamine may increase both systolic and diastolic blood pressure and may counteract the activity of some antihypertensive agents, such as loop diuretics. Close monitoring of blood pressure is advised.
traMADol: (Major) Because of the potential risk and severity of serotonin syndrome, caution should be observed when administering amphetamines with other drugs that have serotonergic properties such as tramadol. Serotonin syndrome is characterized by the rapid development of hyperthermia, hypertension, myoclonus, rigidity, autonomic

instability, mental status changes (e.g., delirium or coma), and in rare cases, death. Further study is needed to fully elucidate the severity and frequency of adverse effects that may occur from concomitant administration of amphetamines and tramadol. Patients receiving tramadol and an amphetamine should be monitored for the emergence of serotonin syndrome, particularly during treatment initiation and during dosage increases. The amphetamine and tramadol should be discontinued if serotonin syndrome occurs and supportive symptomatic treatment should be initiated. In addition, the risk of seizures from the use of tramadol may be increased with concomitant use of CNS stimulants that may induce seizures, including the amphetamines. Extreme caution and close clinical monitoring is recommended if these agents must be used together.
Tramadol; Acetaminophen: (Major) Because of the potential risk and severity of serotonin syndrome, caution should be observed when administering amphetamines with other drugs that have serotonergic properties such as tramadol. Serotonin syndrome is characterized by the rapid development of hyperthermia, hypertension, myoclonus, rigidity, autonomic instability, mental status changes (e.g., delirium or coma), and in rare cases, death. Further study is needed to fully elucidate the severity and frequency of adverse effects that may occur from concomitant administration of amphetamines and tramadol. Patients receiving tramadol and an amphetamine should be monitored for the emergence of serotonin syndrome, particularly during treatment initiation and during dosage increases. The amphetamine and tramadol should be discontinued if serotonin syndrome occurs and supportive symptomatic treatment should be initiated. In addition, the risk of seizures from the use of tramadol may be increased with concomitant use of CNS stimulants that may induce seizures, including the amphetamines. Extreme caution and close clinical monitoring is recommended if these agents must be used together.
Trandolapril: (Minor) Amphetamines increase both systolic and diastolic blood pressure and may counteract the activity of some antihypertensive agents, like angiotensin-converting enzyme inhibitors (ACE inhibitors). Close monitoring of blood pressure is advised.
Trandolapril; Verapamil: (Minor) Amphetamines increase both systolic and diastolic blood pressure and may counteract the activity of some antihypertensive agents, like angiotensin-converting enzyme inhibitors (ACE inhibitors). Close monitoring of blood pressure is advised. (Minor) Amphetamines increase both systolic and diastolic blood pressure and may counteract the activity of some antihypertensive agents, like calcium-channel blockers. Close monitoring of blood pressure is advised.
Tranylcypromine: (Contraindicated) In general, sympathomimetics should be avoided in patients receiving MAOIs due to an increased risk of hypertensive crisis. This applies to sympathomimetics including stimulants for ADHD, narcolepsy or weight loss, nasal, oral, and ophthalmic decongestants and cold products, and respiratory sympathomimetics

(e.g., beta agonist drugs). Some local anesthetics also contain a sympathomimetic (e.g., epinephrine). In general, medicines containing sympathomimetic agents should not be used concurrently with MAOIs or within 14 days before or after their use.
traZODone: (Moderate) Coadministration of trazodone and amphetamines may increase the risk of serotonin syndrome. Serotonin syndrome has been reported with both drugs when taken alone, but especially when coadministered with other serotonergic agents. The MAOI activity of amphetamines may also be of concern with trazodone. Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome. Serotonergic agents should be discontinued if serotonin syndrome occurs and supportive symptomatic treatment should be initiated.
Treprostinil: (Major) Avoid use of sympathomimetic agents with treprostinil. Sympathomimetics counteract the medications used to stabilize pulmonary hypertension, including treprostinil. Sympathomimetics can increase blood pressure, increase heart rate, and may cause vasoconstriction resulting in chest pain and shortness of breath in these patients. Patients should be advised to avoid amphetamine drugs, decongestants (including nasal decongestants) and sympathomimetic anorexiants for weight loss, including dietary supplements. Intravenous vasopressors may be used in the emergency management of pulmonary hypertension patients when needed, but hemodynamic monitoring and careful monitoring of cardiac status are needed to avoid ischemia and other complications.
Triamterene: (Minor) Amphetamines increase both systolic and diastolic blood pressure and may counteract the activity of some antihypertensive agents, like potassium-sparing diuretics. Close monitoring of blood pressure is advised.
Triamterene; hydroCHLOROthiazide, HCTZ: (Minor) Amphetamines increase both systolic and diastolic blood pressure and may counteract the activity of some antihypertensive agents, like potassium-sparing diuretics. Close monitoring of blood pressure is advised. (Minor) Amphetamines may counteract the activity of some antihypertensive agents, such as thiazide diuretics. Close monitoring of blood pressure is advised. Thiazide diuretics may also increase and prolong the actions of amphetamines by increasing the urinary pH.
Tricyclic antidepressants: (Moderate) Monitor blood pressure, heart rate, and for signs and symptoms of serotonin syndrome, particularly during treatment initiation and dosage increase, during concomitant amphetamine and tricyclic antidepressant use. Adjust doses or use alternative therapy based on clinical response. If serotonin syndrome occurs, discontinue therapy. Concomitant use increases the risk for potentiation of cardiovascular effects and serotonin syndrome. Amphetamines may enhance the activity of tricyclic antidepressants causing significant and sustained increases in amphetamine concentrations in the brain.
Trimipramine: (Moderate) Monitor blood pressure, heart rate, and for signs and symptoms of serotonin syndrome, particularly during treatment initiation and dosage

increase, during concomitant amphetamine and tricyclic antidepressant use. Adjust doses or use alternative therapy based on clinical response. If serotonin syndrome occurs, discontinue therapy. Concomitant use increases the risk for potentiation of cardiovascular effects and serotonin syndrome. Amphetamines may enhance the activity of tricyclic antidepressants causing significant and sustained increases in amphetamine concentrations in the brain.
Triprolidine: (Moderate) Amphetamines may pharmacodynamically counteract the sedative properties of some antihistamines, such as the sedating H1-blockers (i.e., diphenhydramine). This effect may be clinically important if a patient is receiving an antihistamine agent for treatment of insomnia. Alternatively, if a patient is receiving an amphetamine for treatment of narcolepsy, the combination with a sedating antihistamine may reverse the action of the amphetamine.
Tromethamine: (Moderate) Monitor for an increase in the incidence and severity of amphetamine-related adverse effects during concomitant use of urinary alkalinizing agents. Increasing urine pH may increase amphetamine exposure by reducing urinary excretion of amphetamine. A urine pH more than 7.5 has been observed to increase the half-life of amphetamine from 8 to 10.5 hours to 16 to 31 hours when compared to a pH less than 6. Additionally, a urine pH more than 8 has been observed to reduce the amount of amphetamine excreted in the urine over 16 hours to less than 3% of the original dose; a 5-fold reduction compared to controls.
Tryptophan, 5-Hydroxytryptophan: (Major) Because of the potential risk and severity of serotonin syndrome, caution should be observed when administering amphetamines with other drugs that have serotonergic properties such as tryptophan. Serotonin syndrome is characterized by the rapid development of hyperthermia, hypertension, myoclonus, rigidity, autonomic instability, mental status changes (e.g., delirium or coma), and in rare cases, death. Further study is needed to fully elucidate the severity and frequency of adverse effects that may occur from concomitant administration of amphetamines and tryptophan. Patients receiving tryptophan and an amphetamine should be monitored for the emergence of serotonin syndrome, particularly during treatment initiation and during dosage increases. The amphetamine and tryptophan should be discontinued if serotonin syndrome occurs and supportive symptomatic treatment should be initiated.
Umeclidinium; Vilanterol: (Moderate) Administer sympathomimetics with caution with beta-agonists such as vilanterol. The cardiovascular effects of beta-2 agonists may be potentiated by concomitant use. Monitor the patient for tremors, nervousness, increased heart rate, or other additive side effects.
Valsartan: (Minor) Amphetamines increase both systolic and diastolic blood pressure and may counteract the activity of some antihypertensive agents, such as angiotensin II receptor antagonists. Close monitoring of blood pressure is advised.
Valsartan; hydroCHLOROthiazide, HCTZ: (Minor) Amphetamines increase both systolic

and diastolic blood pressure and may counteract the activity of some antihypertensive agents, such as angiotensin II receptor antagonists. Close monitoring of blood pressure is advised. (Minor) Amphetamines may counteract the activity of some antihypertensive agents, such as thiazide diuretics. Close monitoring of blood pressure is advised. Thiazide diuretics may also increase and prolong the actions of amphetamines by increasing the urinary pH.
Vasodilators: (Moderate) Use sympathomimetic agents with caution in patients receiving therapy for hypertension. Patients should be monitored to confirm that the desired antihypertensive effect is achieved. Sympathomimetics can increase blood pressure and heart rate, and antagonize the antihypertensive effects of vasodilators when administered concomitantly. Anginal pain may be induced when coronary insufficiency is present.
Venlafaxine: (Moderate) Coadministration of amphetamines with serotonin norepinephrine reuptake inhibitors (SNRIs) may increase the risk of serotonin syndrome. At high doses, amphetamines can increase serotonin release and act as serotonin agonists. Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome, particularly during treatment initiation and dose increases. If serotonin syndrome occurs, serotonergic drugs should be discontinued and appropriate medical treatment should be initiated.
Verapamil: (Minor) Amphetamines increase both systolic and diastolic blood pressure and may counteract the activity of some antihypertensive agents, like calcium-channel blockers. Close monitoring of blood pressure is advised.
Vilazodone: (Moderate) Serotonin syndrome may occur during coadministration of serotonergic drugs such as amphetamines and vilazodone. At high doses, amphetamines can increase serotonin release and act as serotonin agonists. Monitor for the emergence of serotonin syndrome particularly after a dose increase or the addition of other serotonergic medications. Discontinue all serotonergic agents if serotonin syndrome occurs and implement appropriate medical management.
Vonoprazan: (Major) Avoid concomitant use of amphetamines and vonoprazan. Vonoprazan reduces intragastric acidity, which may increase the exposure of amphetamines and risk of toxicity.
Vonoprazan; Amoxicillin: (Major) Avoid concomitant use of amphetamines and vonoprazan. Vonoprazan reduces intragastric acidity, which may increase the exposure of amphetamines and risk of toxicity.
Vonoprazan; Amoxicillin; Clarithromycin: (Major) Avoid concomitant use of amphetamines and vonoprazan. Vonoprazan reduces intragastric acidity, which may increase the exposure of amphetamines and risk of toxicity.
Vortioxetine: (Moderate) Serotonin syndrome may occur during coadministration of serotonergic drugs such as amphetamines and vortioxetine. At high doses, amphetamines can increase serotonin release and act as serotonin agonists. Monitor for

the emergence of serotonin syndrome particularly after a dose increase or the addition of other serotonergic medications to an existing regimen. Discontinue all serotonergic agents if serotonin syndrome occurs and implement appropriate medical management.
Ziprasidone: (Minor) Serotonin syndrome has been reported during the combined use of amphetamine stimulants and other medications with serotonergic properties. Serotonin syndrome has been reported during postmarketing use of ziprasidone; however, a causal relationship has not been established.
ZOLMitriptan: (Moderate) Monitor for signs and symptoms of serotonin syndrome, particularly during treatment initiation and dosage increase, during concomitant serotonin-receptor agonist and amphetamine; dextroamphetamine use. If serotonin syndrome occurs, discontinue therapy. Concomitant use increases the risk for serotonin syndrome.
Zonisamide: (Moderate) Patients who are taking anticonvulsants for epilepsy/seizure control should use amphetamines with caution. Amphetamines may decrease the seizure threshold and increase the risk of seizures. If seizures occur, amphetamine discontinuation may be necessary.

Adverse Reaction

General Information

Adverse side effects of the amphetamines are frequent but usually mild to moderate in children with ADHD at normally prescribed dosages. The side effects may be more frequent or severe with the initial days of therapy.

asthenia, dizziness, drowsiness, dysphemia, dysphoria, euphoria, formication, headache, insomnia, paresthesias, restlessness, supranormalization, tremor

Insomnia is one of the most common centrally-mediated effects of amphetamines. Insomnia will typically resolve within a few days of amphetamine use provided the dosage is appropriate and doses are not administered within 6 hours of bedtime. Avoidance of exercising late in the day, limiting caffeinated beverages, and setting regular bedtime schedules may limit sleep disruption. Continued interrupted sleep patterns may indicate a need for dosage reduction. During clinical trial evaluations of extended-release amphetamine; dextroamphetamine, the following CNS effects were reported in adults and/or pediatric patients: headache (26% of adults), insomnia (27% to 31% of adults, 8% to 12% of adolescents, 17% of children), dizziness (7% of adults, 4% of adolescents, 2% of children), feeling jittery (2% of adults), asthenia (6% of adults, 2% of children), somnolence/drowsiness (2% to 4% of adults), speech disorder (e.g., stuttering or dysphemia, excessive speech, logorrhea) (2% to 4% of adults), twitching (2% to 4% of

adults), and accidental injury (3% of children). Other CNS effects that have been associated with the use of amphetamines include overstimulation, dysphoria, tremor, euphoria, restlessness, and paresthesias (including formication). Children who become overly preoccupied with a task (over-focused or inflexible) or are described as 'zombie-like' are considered to exhibit supranormalization; these behaviors typically require dosage reduction. Once-daily morning dosing of amphetamine; dextroamphetamine is effective in many children and may also help to limit intolerable adverse reactions.

dyskinesia, tics, Tourette's syndrome

Dyskinesia has been reported during postmarketing use of CNS stimulants, including amphetamine; dextroamphetamine products. The onset or exacerbation of motor and verbal tics has also been reported. Individuals should be monitored for the emergence or worsening of dyskinesias, tics, or Tourette syndrome; consider dose reduction or discontinuation of treatment if clinically indicated.

abdominal pain, anorexia, bowel ischemia, constipation, diarrhea, dysgeusia, dyspepsia, nausea, teeth grinding (bruxism), vomiting, weight loss, xerostomia

Anorexia (reported as loss or decrease of appetite) and other appetite changes is one of the most common gastrointestinal (GI) adverse reactions associated with stimulant use. Weight loss is a dose-related adverse effect commonly associated with stimulant use and is of particular concern in growing children and adolescents. In a controlled trial of extended-release amphetamine; dextroamphetamine in adolescents, the mean change in weight during the first 4 weeks of therapy was -1.1 lbs and -2.8 lbs, respectively for patients who received 10 mg and 20 mg daily. An FDA analysis reported children younger than 6 years receiving extended-release stimulants have higher medication exposure and significant weight loss (at least 10% decrease) compared to older children on the same dose. Due to these findings, the benefits may not outweigh the risks in this age group. During clinical trial evaluations of extended-release amphetamine; dextroamphetamine, the following GI effects were reported in adults and/or pediatric patients: loss of appetite (30% to 33% of adults, 22% to 36% of adolescents, 22% of children), weight loss (9% to 10% of adults, 5% to 9% of adolescents, 4% of children), vomiting (7% of children), nausea (8% of adults, 8% of adolescents, 5% of children), diarrhea (3% to 6% of adults), teeth grinding (bruxism) (2% of adults), dyspepsia (2% of children), xerostomia (23% to 35% of adults), constipation (2% to 4% of adults), and abdominal pain (4% to 11% of adolescents, 14% of children). Bowel ischemia has been reported during postmarketing use. Dysgeusia has been associated with the use of amphetamines although the frequency has not been determined. Complaints of xerostomia or dysgeusia may be limited by sucking sugarless hard candy, crushed ice,

and drinking plenty of water or other fluids. Eating small, frequent meals or snacks may help limit gastrointestinal effects.

growth inhibition

Growth inhibition is a possible long-term side effect of the use of stimulants in children and adolescents; proposed mechanisms have included the suppression of appetite or an alteration in growth hormone secretion. Some have suggested that the use of drug holidays will allow growth to 'catch-up'. However, drug holidays are typically reserved for children with well-controlled ADHD symptoms, and drug holidays are of unproved value in limiting growth suppression. Growth rebound has been observed after the discontinuation of the stimulants in children and clinical studies do not indicate that amphetamines compromise the attainment of normal adult height and weight. However, practitioners should monitor for this side effect by monitoring height and weight parameters relative to age at the initiation of treatment and periodically during therapy (at minimum yearly). Patients who are not growing or gaining weight as expected may need to have their treatment interrupted. In a 24-month follow-up, the Multimodal Treatment Study showed a deceleration of growth of roughly 1 cm per year with stimulant use. In general, growth remained in the normal curve for most children, except those in the lowest percentiles of height for age. Data obtained on the effects of stimulants on growth suppression in children 7 to 10 years suggested that regularly medicated children (7 days/week) had a temporary average slowing in growth of 2 cm in height and 2.7 kg in weight over 3 years; it is anticipated that chronic amphetamine use may cause similar suppression.

arrhythmia exacerbation, bradycardia, cardiomyopathy, chest pain (unspecified), dyspnea, hypertension, hypotension, myocardial infarction, palpitations, sinus tachycardia, stroke, syncope

Like other stimulant medications, amphetamine; dextroamphetamine is associated with cardiovascular adverse effects ranging in severity from mild to fatal. In normal therapeutic doses, amphetamines may induce increases in both systolic and diastolic blood pressure and exacerbate hypertension. In a single dose pharmacokinetic study of adolescents with ADHD (n = 23), increases in systolic blood pressure above the upper 95% CI for age, gender, and stature occurred in 12% of patients given 10 mg of extended-release amphetamine;dextroamphetamine (Adderall XR) and 35% of patients given 20 mg. Maximal increases occurred 2 to 4 hours after dosing, were transient, and were not associated with symptoms. In a second study of adolescents with ADHD treated over a 4-week period, systolic blood pressure increases (15 mmHg or more) occurred in 7% of patients receiving Adderall XR (n = 100) and 11% of patients receiving placebo (n = 64). Diastolic blood pressure increases (8 mmHg or more) occurred in 22%

of patients receiving Adderall XR and 25% of patients receiving placebo. In general, stimulant medications cause an average increase in blood pressure of about 2 to 4 mmHg. A reflex sinus bradycardia, which is not usually clinically significant, may occur. In general, stimulant medications increase heart rate by an average of 3 to 6 bpm, but some patients may experience significantly higher increases. During clinical trial evaluations of extended-release amphetamine; dextroamphetamine in adults, the following cardiac effects were reported more frequently in patients receiving extended-release amphetamine; dextroamphetamine than placebo: tachycardia (6%), increased heart rate (9%), dyspnea (2% to 4%), and palpitations (2% to 4%). Other cardiovascular-related events that have been reported with the use of amphetamines include sudden death, myocardial infarction, stroke (unspecified), and isolated cases of cardiomyopathy with chronic administration. Sudden cardiac death has also been reported in association with CNS stimulant treatment at usual doses in children, adolescents, and adults with structural cardiac abnormalities and other serious heart conditions. Although some structural cardiac abnormalities alone may carry an increased risk of sudden death, stimulant products generally should not be used in children, adolescents, or adults with known structural cardiac abnormalities or other serious heart conditions. All patients should be advised of the risk of serious cardiovascular events (e.g., arrhythmia or arrhythmia exacerbation, tachycardia, hypertension, hypotension) with stimulant use. Patients who develop symptoms such as exertional chest pain (unspecified), unexplained syncope, or other symptoms suggestive of cardiac disease during amphetamine; dextroamphetamine treatment should undergo a prompt cardiac evaluation.

dysmenorrhea, impotence (erectile dysfunction), libido decrease, libido increase, priapism

During clinical trial evaluations of extended-release amphetamine; dextroamphetamine in adults, the following genitourinary effects were reported more frequently in patients receiving extended-release amphetamine; dextroamphetamine than placebo: dysmenorrhea (2% to 4%), libido decrease (2% to 4%), and impotence (erectile dysfunction) (2% to 4%). Frequent or prolonged erections have occurred during administration of amphetamine derivatives. Similar reactions, including priapism, have been reported during use of other ADHD medications such as methylphenidate and atomoxetine. Reported cases of priapism have occurred after a period of time on stimulant therapy and often subsequent to a dose increase. Priapism has also been reported during periods of drug withdrawal (e.g., drug holidays or discontinuation). Prolonged erections in male patients should be promptly reported, as immediate diagnosis and treatment are essential to avoid tissue damage. Amphetamines have been reported to occasionally cause libido increase.

seizures

Stimulant medications have the potential to lower the seizure threshold in patients with a prior history of seizures, in patients with a history of EEG abnormalities without a history of seizures, and rarely in patients without a seizure history or EEG abnormalities. Stimulant medications should be discontinued if seizures develop. Seizures are also associated with amphetamine; dextroamphetamine toxicity; carefully evaluate the patient for other signs and symptoms of overdose if seizures occur.

alopecia, anaphylactoid reactions, angioedema, hyperhidrosis, photosensitivity, rash, Stevens-Johnson syndrome, toxic epidermal necrolysis, urticaria

Dermatologic and allergic reactions to amphetamines are rare, however serious events such as angioedema, anaphylactoid reactions, Stevens-Johnson syndrome, and toxic epidermal necrolysis have all been reported with the use of amphetamine or amphetamine derivatives. During clinical trial evaluation of extended-release amphetamine; dextroamphetamine in adults, hyperhidrosis and photosensitivity reaction occurred in 2% to 4% of patients receiving extended-release amphetamine; dextroamphetamine and at a greater frequency than placebo. Urticaria, rash (unspecified), and alopecia have also been reported during the administration of amphetamines.

blurred vision, mydriasis, visual impairment

Visual impairment, including blurred vision, difficulties with visual accommodation, and mydriasis, has been reported during postmarketing use of amphetamines. Patients are encouraged to report any unusual changes in vision promptly for examination and evaluation.

peripheral vasoconstriction, skin ulcer

Stimulants used to treat ADHD, including amphetamine; dextroamphetamine, are associated with peripheral vasculopathy. Effects of peripheral vasoconstriction, including Raynaud's phenomenon, were observed in postmarketing reports at therapeutic doses in all age groups throughout the course of treatment. Signs and symptoms are usually intermittent and mild and generally improve after reduction in dose or discontinuation of drug. However, very rare sequelae include digital skin ulcer and/or soft tissue breakdown. Carefully monitor for digital changes during treatment with ADHD stimulants. Further clinical evaluation (e.g., rheumatology referral) may be appropriate for certain patients.

agitation, anxiety, depression, emotional lability, hallucinations, hostility, irritability, mania, psychosis, suicidal ideation

Stimulant medications, such as amphetamine; dextroamphetamine, can cause psychotic or manic symptoms (i.e., hallucinations, delusional thinking, or mania) in patients without a prior history of psychosis or mania, and have occurred during use of recommended doses and with toxicity or abuse. These symptoms occurred in approximately 0.1% of patients treated with stimulants (methylphenidate or amphetamine at usual doses) compared to 0% in placebo-treated patients in a pooled analysis of short-term, placebo-controlled studies. In a cohort study assessing 221,846 adolescents and young adults who received a prescription for a stimulant for ADHD, new-onset psychosis occurred in approximately 1 in 660 patients. The percentage of patients who had a psychotic episode was 0.1% in patients receiving methylphenidate compared to 0.21% in patients receiving amphetamine (hazard ratio with amphetamine use, 1.65; 95% CI 1.31 to 2.09). The median time from when the stimulant was dispensed to the psychotic episode was 128 days. Aggression, hostility, and suicidal ideation or behaviors have also been reported during the use of medications for ADHD. Although causality to the drugs has not been established and these behaviors are often observed in children and adolescents with ADHD, close monitoring is recommended. If suicide-related events emerge during treatment, consideration should be given to dose reduction or drug discontinuation, especially if symptoms are severe, abrupt in onset, or were not part of the patient's presenting symptoms. During clinical trial evaluation of extended-release amphetamine; dextroamphetamine, the following psychiatric effects occurred in adults and/or pediatric patients: anxiety (7% to 8% of adults), nervousness (13% of adults, 6% of adolescents, 6% of children), irritability (6% of adolescents), emotional lability (2% to 4% of adults, 9% of children), depression (3% of adults), and agitation (2% to 8% of adults). Other psychiatric effects that have been associated with the use of amphetamine; dextroamphetamine include anger and dermatillomania. Patients and their caregivers should be advised to promptly report any changes in mood or behavior. Discontinuation of the drug may be required if psychiatric symptoms are persistent or severe. Abrupt discontinuation of amphetamines after chronic administration may unmask severe depression, suicidal ideation, anxiety, agoraphobia, dysphoria, psychomotor agitation, or symptoms of overactive behaviors.

coma, confusion, delirium, hyperreflexia, hyperthermia, paranoia, renal failure (unspecified), rhabdomyolysis, tachypnea

Toxic effects of amphetamines are more variable in children than in adults and appear to occur over a wide dosage range. Signs of excessive dosages or acute overdose may include: anxiety, headache, euphoria, hyperactivity, agitation, confusion, delirium,

paranoia, hallucinations, tremor, paresthesias, palpitations, sinus tachycardia, hypertension, chest pain (unspecified), nausea, vomiting, diaphoresis, mydriasis, dyspnea, tachypnea, hyperthermia, and hyperreflexia. Minor manifestations of any of these symptoms during prescription use indicate a need for dosage reduction or discontinuation. Severe manifestations of amphetamine overdose include cardiac arrhythmias, refractory hypotension, myocardial infarction, circulatory collapse, ischemic stroke, rhabdomyolysis, seizures, acute renal failure (unspecified), fulminant hyperthermia, coma, and death. Symptoms of chronic intoxication with amphetamines include severe dermatoses, marked insomnia, irritability, hyperactivity, and psychosis indistinguishable from schizophrenia. Some severe manifestations of toxicity may also occur during therapeutic use of amphetamines, such as rhabdomyolysis, seizures, cardiac arrhythmias, and psychosis; however, they are most often associated with sympathomimetic toxicity. The product labeling for amphetamines includes a boxed warning stating that misuse of amphetamines may cause sudden death or serious cardiovascular adverse events.

serotonin syndrome

Amphetamines stimulate the release of serotonin (5-HT) and may act as direct agonists on central serotonin receptors. Thus, amphetamines are both direct and indirect stimulants of serotonin activity. Serotonin syndrome may occur when amphetamines are combined with other medications (e.g., SSRIs) that enhance serotonin activity within the CNS or following overdose. Serotonin syndrome is characterized by the rapid development of hyperthermia, hypertension, myoclonus, rigidity, autonomic instability, mental status changes (e.g., agitation, delirium, hallucinations, coma), and in rare cases, death. The use of amphetamines with potent CYP2D6 inhibitors, such as paroxetine or fluoxetine, may also increase the risk through inhibition of amphetamine metabolism and an increase in systemic exposure. If serotonin syndrome becomes evident during treatment, the amphetamine and any other serotonergic agents should be discontinued and appropriate medical treatment should be initiated.

physiological dependence, psychological dependence, tolerance, withdrawal

Psychological dependence, physiological dependence, and tolerance may occur with amphetamine; dextroamphetamine therapy. Abrupt discontinuation or a significant dose reduction of CNS stimulants after prolonged use may produce withdrawal symptoms that include dysphoria, depression, fatigue, vivid and unpleasant dreams, insomnia or hypersomnia, increased appetite, and psychomotor retardation or agitation. Signs and symptoms of chronic amphetamine abuse include severe

dermatoses, marked insomnia, irritability, hyperactivity, personality changes, and psychosis with features indiscriminate from schizophrenia.

dental caries, fever, infection

Patients receiving extended-release amphetamine; dextroamphetamine salts in clinical trials experienced fever (5% of children), infection (3% of children), viral infection (1% of adolescent patients) and urinary tract infection (5% of adults). Other infections occurring in 2% to 4% of adults receiving extended-release amphetamine; dextroamphetamine and at a greater frequency than placebo included tooth infection (dental caries).

laboratory test interference

Amphetamines can cause a significant elevation in plasma corticosteroid levels; this increase is greatest in the evening. Amphetamines may cause laboratory test interference with urinary steroid determinations. These effects may need to be considered during testing.

Description

Amphetamine and dextroamphetamine mixed salts are used in combination as an oral preparation to treat attention-deficit hyperactivity disorder (ADHD) or narcolepsy. Stimulants are considered first-line agents in the treatment of ADHD. Amphetamine- and methylphenidate-containing products are considered equally effective in the treatment of ADHD; patients who do not respond to one may respond to the other. The most common adverse reactions associated with amphetamine use include anorexia, abdominal pain, irritability, restlessness, insomnia, emotional lability, and tachycardia. Stimulants can induce or exacerbate psychiatric symptoms and should be used with caution in patients with a history of mania, psychosis, or substance abuse. Stimulant use has also been associated with new or worsening tics or worsening Tourette's syndrome. Close monitoring for the emergence or worsening of psychiatric symptoms, tics, or Tourette's syndrome is recommended. Stimulants have also been associated with sudden death in patients with structural cardiac abnormalities or other serious cardiac disease when used at recommended ADHD doses; patients with structural heart defects, cardiomyopathy, coronary artery disease, serious cardiac arrhythmias, or other serious cardiac disease may be at risk for adverse cardiac events. The American Academy of Pediatrics and the American Heart Association recommend careful screening of all children and adolescents prior to initiating pharmacologic therapy for ADHD, including a detailed patient and family history and physical examination; any significant findings should be further assessed and referred for consultation with a pediatric cardiologist prior to initiating treatment.

Mechanism Of Action

Amphetamines are non-catecholamine sympathomimetic amines with CNS stimulant activity. Amphetamine and dextroamphetamine stimulate the release of norepinephrine (NE) and other biologic amines from central adrenergic receptors. At higher dosages, they cause release of dopamine (DA) from the mesocorticolimbic system and the nigrostriatal dopamine systems. It is thought that the release of dopamine is responsible for the reinforcing properties of amphetamine. At still higher doses, amphetamine stimulates the release of 5-hydroxytryptamine (5-HT). Finally, amphetamine may act as a direct agonist on central 5-HT receptors. Thus, amphetamine is both a direct and an indirect stimulant. Amphetamines may also inhibit monoamine oxidase (MAO), but this is a minor action. Dextroamphetamine exhibits greater CNS stimulation than racemic- or levo- amphetamine on a weight basis. Amphetamine-induced CNS stimulation produces a decreased sense of fatigue, an increase in motor activity and mental alertness, mild euphoria, and brighter spirits. Lithium may offset amphetamine-induced euphoria. Actions in ADHD: The mode of therapeutic action in Attention Deficit Hyperactivity Disorder (ADHD) is not known. Improved attention spans, decreased distractibility, increased ability to follow directions or complete tasks, and decreased impulsivity and aggression have been noted when stimulants are prescribed for the treatment of ADHD. Peripheral actions: In the periphery, the actions of amphetamines are believed to occur through release of norepinephrine from the adrenergic nerve terminals and by a direct stimulant action on alpha- and beta-receptors. Dextroamphetamine has less peripheral activity than racemic amphetamine at normally prescribed dosages. Amphetamines increase systolic and diastolic blood pressure and cause respiratory stimulation and weak bronchodilation. Heart rate typically increases slightly with normal therapeutic doses of stimulants (about 3 to 6 bpm); however, a reflexive decrease in heart rate in response to increased blood pressure can also occur. At high doses, such as in overdoses, amphetamine and its derivatives can cause significant hypertension, tachycardia, arrhythmias, and other serious complications. Amphetamines may produce mydriasis and contraction of the bladder sphincter.

Pharmacokinetics

Amphetamine and dextroamphetamine mixed salts are administered orally. Commercially available products contain d-amphetamine and l-amphetamine salts in the ratio of 3:1. Amphetamine; dextroamphetamine is widely distributed throughout the body, including the central nervous system (CNS). Volume of distribution (Vd) increases as body weight increases. Amphetamine is reported to be oxidized at the 4 position of the benzene ring to form 4-hydroxyamphetamine, or on the side chain alpha- or beta-

carbons to form alpha-hydroxy-amphetamine or norephedrine, respectively. Norephedrine and 4-hydroxy-amphetamine are both active and each is subsequently oxidized to form 4-hydroxy-norephedrine. Alpha-hydroxy-amphetamine undergoes deamination to form phenylacetone, which ultimately forms benzoic acid and its glucuronide and the glycine conjugate hippuric acid. The specific enzymes involved in amphetamine metabolism have not been described; however, the formation of 4-hydroxy-amphetamine is known to involve CYP2D6. Since CYP2D6 is genetically polymorphic, variations in amphetamine metabolism are a possibility. Children exhibit a higher clearance than adolescents and adults when adjusted for body weight. Under normal conditions, the plasma half-life of amphetamine; dextroamphetamine mixed salts (Adderall and Adderall XR) is roughly 9 to 11 hours in children 6 years and older, 11 to 14 hours in adolescents, and 10 to 13 hours in adults. In both pediatric and adult patients receiving amphetamine; dextroamphetamine mixed salts (Mydayis), the mean plasma elimination half-life for d-amphetamine ranges from about 10 to 11 hours and l-amphetamine from 10 to 13 hours.

Amphetamines and their metabolites are excreted in the urine. With normal urine pH, approximately 30% to 40% of the administered dose is recoverable in urine as amphetamine and 50% as alpha-hydroxy-amphetamine (inactive metabolite). Since amphetamine has a pKa of 9.9, urinary recovery of amphetamine is highly dependent on pH and urine flow rates. Alkaline urine pHs result in less ionization and reduced renal elimination of amphetamine. Conversely, acidification of the urine and high urinary flow rates result in increased renal elimination with clearances greater than glomerular filtration rates, indicating the involvement of active secretion. Urinary recovery of amphetamine has been reported to range from 1% to 75% depending on urinary pH. The urinary elimination of amphetamines and their metabolites may be affected by agents that acidify or alkalinize the urinary fluids.

Possibly affected cytochrome P450 isoenzymes and drug transporters: CYP2D6
The specific enzymes involved in amphetamine metabolism have not been described; however, the formation of 4-hydroxy-amphetamine is known to involve CYP2D6. Because CYP2D6 is genetically polymorphic, variations in amphetamine metabolism are a possibility. Amphetamines are not an in vitro inhibitor of CYP1A2, CYP2C9, CYP2C19, CYP2D6, or CYP3A, nor an in vitro inducer of CYP1A2, CYP2B6, or CYP3A4/5. Amphetamines are not an in vitro substrate for P-glycoprotein (P-gp).

Route-Specific Pharmacokinetics

- **Oral Route**

Immediate-release tablets
After oral administration, peak plasma concentrations occur approximately 3 hours

post-dose. The effect of food on the bioavailability of immediate-release tablets has not been studied.

Extended-release capsules (Adderall XR)
After oral administration, the maximum systemic absorption of extended-release capsules is completed within 7 hours compared to 3 hours for immediate-release tablets. In a pharmacokinetic study assessing 51 children with attention-deficit hyperactivity disorder (ADHD), after initial exposure to extended-release 20 mg capsules, mean maximum plasma concentration (Cmax) was 40.1 ng/mL for the d-isomer and 11.89 ng/mL for the l-isomer, consistent with the 3:1 ratio found in the parent compound. At steady state, mean Cmax reported was 47.22 ng/nL and 14.92 ng/nL for the d- and l-isomers, respectively. Area under the curve (AUC) and Cmax decreases with increases in body weight; children have a higher systemic exposure when compared to adults. However, based upon dose normalization on a mg/kg basis, children show approximately 30% less systemic exposure compared to their adult counterparts. Sprinkling extended-release capsules on applesauce gives comparable plasma concentrations to administration of the intact capsule in the fasted state. Otherwise, food does not affect the extent of absorption of amphetamine, but prolongs Tmax by approximately 2.5 hours. Pharmacokinetic parameters are linear over the normal dosage range.

Extended-release capsules (Mydayis)
After oral administration, peak plasma concentrations occurred in about 7 to 10 hours in adolescents (13 to 17 years) and about 8 hours in adults (19 to 51 years) for both d-amphetamine and l-amphetamine. Pharmacokinetic parameters are linear over the normal dosage range. Steady-state is achieved between days 7 and 8 of dosing with mean accumulation ratio of 1.6. Body weight is the primary determinant of apparent differences in pharmacokinetics across the age range. Based on dose proportionality, a single dose administered to adolescents would produce about 21% to 31% higher Cmax and AUC for d- and l-amphetamine, compared to the same dose administered to adults. Administration with a high-fat meal does not affect the extent of absorption, but prolongs the Tmax by 5 hours (7 hours at fasted state to 12 hours after a high-fat meal) for d-amphetamine and 4.5 hours (7.5 hours at fasted state to 12 hours after a high-fat meal) for l-amphetamine. Sprinkling on applesauce results in comparable absorption and exposure to the intact capsule taken in the fasted state. The presence of alcohol potentially increases release of amphetamine. At an alcohol concentration of 20% or 40%, in vitro testing showed increases in amphetamine release rate. There is no in vivo study for the effect of alcohol on drug exposure.

- **Hepatic Impairment**

Hepatic dysfunction has the potential to inhibit the elimination of amphetamine and result in prolonged exposures.

- **Renal Impairment**

Renal dysfunction has the potential to inhibit the elimination of amphetamine and result in prolonged exposures. Dextroamphetamine is not dialyzable. Use in patients with end-stage renal disease is not recommended.

- **Pediatrics**

Extended-release capsules (Adderall XR)
Children and Adolescents 6 years and older
Children exhibit a higher clearance than adolescents and adults when adjusted for body weight. Under normal conditions, the plasma half-life of amphetamine; dextroamphetamine is roughly 9 to 11 hours in children 6 years and older, 11 to 14 hours in adolescents, and 10 to 13 hours in adults. However, children exhibit higher systemic exposure to amphetamine (based on Cmax and AUC) than adults for a given dose of extended-release amphetamine; dextroamphetamine; this difference is attributed to the higher dose administered to children on a mg/kg basis. Upon dose-normalization on a mg/kg basis, children showed 30% less systemic exposure when compared to adults.

Extended-release capsules (Mydayis)
Adolescents 13 years and older
Body weight is the primary determinant of apparent pharmacokinetic differences in adolescents (13 to 17 years old) compared to adult patients (19 to 62 years). Based on dose proportionality, a single dose administered to adolescents would produce about 21% to 31% higher Cmax and AUC for d- and l-amphetamine, compared to the same dose administered to adults.

- **Gender Differences**

Systemic exposure to amphetamines is 20% to 30% higher in females as compared to males, but differences diminish when females are given weight-based dosing comparable to male subjects. Gender had no direct effect on the pharmacokinetics of d-amphetamine or l-amphetamine.

- **Ethnic Differences**

Race does not appear to influence the pharmacokinetics of the amphetamines.

Administration

For storage information, see the specific product information within the How Supplied section.

Oral Administration

Oral Solid Formulations

Immediate-release tablets:
Administer the first dose of the day upon awakening.
Subsequent doses during the day, if given, should be administered at least 6 hours before bedtime to avoid sleep interference.

Extended-release capsules (Adderall XR):
Administer dose once daily in the morning upon awakening. Swallow whole, do not crush, cut, or chew the capsule or capsule contents (beads).
If swallowing is difficult, the capsule may be opened and the entire contents gently sprinkled on a spoonful of cool applesauce and swallowed immediately (do not store for future use). Follow with a drink of water or other liquid.
Do not divide the dose of a single capsule.

Extended-release capsules (Mydayis):
Administer dose once daily in the morning upon awakening consistently either with or without food. Swallow whole, do not crush, cut, or chew the capsule or capsule contents (beads).
If swallowing is difficult, the capsule may be opened and the entire contents gently sprinkled on a spoonful of applesauce and swallowed immediately (do not store for future use).
Do not divide the dose of a single capsule.

Maximum Dosage Limits

- **Adults**
  For immediate-release tablets, 40 mg/day PO for ADHD (doses up to 60 mg/day PO have been used for weight more than 50 kg) or 60 mg/day PO for narcolepsy. For extended-release Adderall XR capsules, 20 mg/day PO is the recommended dose; in clinical trials for adult ADHD, 60 mg/day PO was the highest titration dose used. For extended-release Mydayis capsules, 50 mg/day PO for ADHD.
- **Geriatric**
  For immediate-release tablets, 60 mg/day PO for narcolepsy; geriatric patients have not been evaluated for ADHD. For extended-release capsules, geriatric patients have not been evaluated.
- **Adolescents**

For immediate-release tablets, 40 mg/day PO for ADHD (doses up to 60 mg/day PO have been used for weight more than 50 kg) or 60 mg/day PO for narcolepsy. In clinical trials of extended-release Adderall XR capsules, titration doses were allowed up to 40 mg/day PO for weight 75 kg or less and from 50 to 60 mg/day PO for weight more than 75 kg; however, there was no consistent evidence that doses above 20 mg/day PO conferred additional benefit. For extended-release Mydayis capsules, 25 mg/day PO for ADHD.

- **Children**
  6 years and older: For immediate-release tablets, 40 mg/day PO for ADHD (doses up to 60 mg/day PO have been used for weight more than 50 kg) or 60 mg/day PO for narcolepsy. For extended-release Adderall XR capsules, 30 mg/day PO for ADHD. For extended-release Mydayis capsules, safety and efficacy have not been established.
  3 to 5 years: Maximum dosage information is not provided by FDA-approved labeling; doses should not exceed 40 mg/day PO for immediate-release tablets. Do not use extended-release capsules.
  Less than 3 years: Safety and efficacy have not been established.
- **Infants**
  Not indicated.

Dosage Forms

- Adderall XR 25mg Extended-Release Capsule
- Adderall XR 30mg Extended-Release Capsule
- Adderall XR 5mg Extended-Release Capsule
- Amphetamine Aspartate 1.25mg, Amphetamine Sulfate 1.25mg, Dextroamphetamine Saccharate 1.25mg, Dextroamphetamine Sulfate 1.25mg Oral capsule, biphasic release
- Amphetamine Aspartate 6.25mg, Amphetamine Sulfate 6.25mg, Dextroamphetamine Saccharate 6.25mg, Dextroamphetamine Sulfate 6.25mg Oral capsule, biphasic release
- Amphetamine Aspartate 7.5mg, Amphetamine Sulfate 7.5mg, Dextroamphetamine Saccharate 7.5mg, Dextroamphetamine Sulfate 7.5mg Oral capsule, biphasic release

Dosage Adjustment Guidelines

Hepatic Impairment

Specific guidelines for dosage adjustments in hepatic impairment are not available; the FDA-approved product labeling states that hepatic dysfunction has the potential to inhibit the elimination of amphetamine and result in prolonged exposures; use caution.

Renal Impairment

Immediate-release products:
Specific guidelines for dosage adjustments of immediate-release products in renal impairment in adults and pediatric patients are not available; the FDA-approved product labeling states that renal dysfunction has the potential to inhibit the elimination of amphetamine and result in prolonged exposures; use caution.

ADULT RENAL DOSE ADJUSTMENTS
Adult renal dose adjustments for extended-release capsules (Adderall XR)
eGFR 15 to 29 mL/minute/1.73 m2: 15 mg PO once daily in the morning.
eGFR less than 15 mL/minute/1.73 m2: Initiation of extended-release capsules (Adderall XR) is not recommended.

Adult renal dose adjustments for extended-release capsules (Mydayis)
eGFR 15 to 29 mL/minute/1.73 m2: Starting dose is is 12.5 mg PO once daily. Maximum dose is 25 mg PO once daily.
eGFR less than 15 mL/minute/1.73 m2: Initiation of extended-release capsules (Mydayis) is not recommended.

PEDIATRIC RENAL DOSE ADJUSTMENTS
Pediatric renal dose adjustments (6 to 17 years of age) for extended-release capsules (Adderall XR)
eGFR 15 to 29 mL/minute/1.73 m2: 5 mg PO once daily is the recommended dose. The maximum dose for children 6 to 12 years of age is 20 mg PO once daily.
eGFR less than 15 mL/minute/1.73 m2: Initiation of extended-release capsules (Adderall XR) is not recommended.

Pediatric renal dose adjustments (13 to 17 years of age) for extended-release capsules (Mydayis)
eGFR 15 to 29 mL/minute/1.73 m2: Starting and maximum dose is is 12.5 mg PO daily.
eGFR less than 15 mL/minute/1.73 m2: Initiation of extended-release capsules (Mydayis) is not recommended.