COLMAN

1.1 Product Name : Generic Name or International Non –Proprietary Name (INN)

Chlorpheniramine Maleate & Phenylephrine capsules....

1.2 Dosage Strength

Composition :

Each Capsules Contains

Chlorpheniramine Maleate BP ……..4 mg

Phenylephrine Hydrochloride BP……..2.5 mg.

1.3 Dosage Form :

Oral Capsules.

2) Pharmaceutical Form

Pink/ CT capsules containing Multi-coloured Pellets.

3)Clinical Particulars

Oral sedating antihistamine and decongestant combination Used for relief of upper respiratory symptoms such as nasal congestion, rhinorrhea, and sneezing associated with allergic or vasomotor rhinitis, the common cold, or sinusitis.

3.1 Therapeutic Indications :

For temporary relief of symptoms due to the common cold, allergic rhinitis, or other upper respiratory allergies (e.g., rhinorrhea, nasal congestion, sneezing, itchy, watery eyes, itching of the nose or throat).

Oral dosage (immediate-release tablets with chlorpheniramine HCl 3, 3.5, or 4 mg and phenylephrine HCl 10 mg per tablet)
Adults, Adolescents and Children 12 years and older

1 tablet PO every 4 to 6 hours as needed. Do not exceed 6 tablets in 24 hours.

Children 6 to 11 years

One-half tablet PO every 4 to 6 hours as needed. Do not exceed 3 tablets in 24 hours.

Oral dosage (oral liquid containing chlorpheniramine maleate 1 mg; phenylephrine HCl 2.5 mg in 5 mL; e.g., Triaminic Cold and Allergy)
Children 6 to 11 years

10 mL PO every 4 hours, not to exceed 6 doses in 24 hours.

Oral dosage (oral solution with chlorpheniramine maleate 1 mg; phenylephrine hydrochloride 2.5 mg per 1 mL; e.g., DAllergy Drops)
Adults, Adolescents, and Children 12 years and older

4 mL PO every 4 hours as needed. Do not exceed 6 doses in 24 hours.

Children 6 to 11 years

2 mL PO every 4 hours as needed. Do not exceed 6 doses/24 hours.

Oral dosage (oral liquid containing chlorpheniramine maleate 4 mg; phenylephrine hydrochloride 10 mg in 5 mL; e.g., Ed A-Hist Liquid)
Adults and Adolescents

5 mL PO 3 to 4 times per day.

Children 6 to 12 years

2.5 mL PO 3 to 4 times per day.

Children 2 to 5 years

1.25 mL PO 3 to 4 times per day.

Oral dosage (extended-release capsules containing chlorpheniramine maleate 4 mg; phenylephrine hydrochloride 20 mg; e.g., Dallergy-Jr Capsules)

Adults and Adolescents

2 capsules PO every 12 hours, not to exceed 2 doses in 24 hours.

Children 6 to 12 years

1 capsule PO every 12 hours, not to exceed 2 doses in 24 hours.

Oral dosage (tablets containing chlorpheniramine tannate 8 mg; phenylephrine tannate 25 mg; e.g., Ricobid)

Adults

3.2 Dosage :

Do not exceed recommended dosage limits for the specific product prescribed/used; the following are general guidelines:

Adults

Chlorpheniramine 24 mg/day PO; phenylephrine 80 mg/day PO.

Geriatric

Chlorpheniramine 24 mg/day PO; phenylephrine 80 mg/day PO.

Adolescents

Chlorpheniramine 24 mg/day PO; phenylephrine 80 mg/day PO.

Children

12 years: Chlorpheniramine 24 mg/day PO; phenylephrine 80 mg/day PO.

6 to 11 years: Chlorpheniramine 12 mg/day PO; phenylephrine 40 mg/day PO.

2 to 5 years: Most products not for this age group. See specific product label for dosing (prescription products).

Less than 2 years: Safety and efficacy have not been established.

Infants

Safety and efficacy have not been established.

DOSING CONSIDERATIONS

Hepatic Impairment

Specific guidelines for dosage adjustments in hepatic impairment are not available; however, lower doses may be warranted due to decreased metabolism of one or both ingredients.

Renal Impairment

Dosage adjustments may be warranted; however, specific guidelines in renal impairment are not available.

ADMINISTRATION

Oral Administration

Chlorpheniramine; phenylephrine may be administered without regard to meals. May be taken with food or milk to minimize GI irritation.

Oral Solid Formulations

3.1 CONTRAINDICATIONS / PRECAUTIONS

General Information

Patients known to be hypersensitive to other sympathomimetic amines may exhibit cross-sensitivity to phenylephrine.

Driving or operating machinery

Chlorpheniramine; phenylephrine may cause sedation, therefore, patients should be advised to avoid driving or operating machinery until they know how this product will affect them. Patients should be informed that alcohol consumption may intensify the sedative effects of the drug.

Asthma, bronchitis, chronic obstructive pulmonary disease (COPD), emphysema, pulmonary disease, status asthmaticus

Products containing an H1-antagonist, such as chlorpheniramine, should be used with caution in those with pulmonary disease, including asthma, chronic bronchitis, and emphysema. The anticholinergic activity of H1-antagonists may result in thickened bronchial secretions thereby aggravating an acute asthmatic attack or chronic obstructive pulmonary disease (COPD). Although antihistamine-containing products, such as chlorpheniramine; phenylephrine, are contraindicated during an acute asthmatic attack (status asthmaticus), their anticholinergic effects do not preclude their use in all patients with asthma or COPD.

Hepatic disease

Chlorpheniramine and phenylephrine are metabolized in the liver. It is, therefore, possible that metabolism of one or both of these medications may be reduced in those with significant hepatic disease. Monitoring of liver function tests should be considered in this patient population. Dosage adjustments may be required, as drug accumulation or prolonged duration of action may be possible in patients with hepatic dysfunction.

Renal disease, renal failure, renal impairment

The effects of using chlorpheniramine; phenylephrine combination products in patients with renal disease, renal impairment, or renal failure are unknown. However, drug accumulation or prolonged duration of action may be possible in those with renal dysfunction. The half-life of chlorpheniramine when used as a single agent in chronic renal failure patients undergoing dialysis may be as long as 280—330 hours. Dosage adjustments in the presence of renal disease may be necessary.

Acute myocardial infarction, angina, atrial fibrillation, atrial flutter, AV block, bradycardia, bundle-branch block, cardiac arrhythmias, cardiac disease, cardiomyopathy, coronary artery disease, heart failure, hypertension, myocardial infarction, tachycardia, ventricular fibrillation, ventricular tachycardia

Various adverse cardiovascular effects are possible following administration of chlorpheniramine; phenylephrine. Phenylephrine is contraindicated in patients with severe or uncontrolled hypertension, and cardiac arrhythmias associated with tachycardia (e.g., atrial fibrillation, atrial flutter, ventricular fibrillation, ventricular tachycardia) because of its detrimental cardiovascular effects in these conditions (i.e., increased myocardial oxygen demand, chronotropy, proarrhythmic potential, and vasoactivity); it should be used with caution in patients with coronary artery disease (e.g., angina, history of myocardial infarction, acute myocardial infarction). Products with phenylephrine and chlorpheniramine should be used with considerable caution in patients with bradycardia, partial heart block (AV block, bundle-branch block), controlled or mild hypertension, heart failure, cardiomyopathy, ischemic heart disease, or other cardiac disease due to the sympathomimetic effects of phenylephrine and quinidine-like local anesthetic and anticholinergic effects of chlorpheniramine.

Aneurysm, arteriosclerosis, cerebrovascular disease, intracranial bleeding, organic brain syndrome, stroke

Products containing phenylephrine should be avoided if possible in patients with cerebrovascular disease such as cerebral arteriosclerosis, aneurysm, intracranial bleeding, history of stroke, or organic brain syndrome because of the potential sympathomimetic (presumably alpha) effects in the CNS and the potential for cerebrovascular hemorrhage.

Children, infants, neonates

Most chlorpheniramine; phenylephrine products are labeled only for use in children 6 years of age and older. The use of chlorpheniramine; phenylephrine in neonates is contraindicated. Antihistamines may cause paradoxical CNS stimulation or seizures, especially in neonates. The adverse effects of sympathomimetic agents can be severe, especially in infants and young children; CNS stimulation, increased blood pressure, and tachycardia may occur. Pediatric patients receiving chlorpheniramine; phenylephrine should be closely monitored. In January 2007, the CDC warned caregivers and healthcare providers of the risk for serious injury or fatal overdose from the administration of cough and cold products to children and infants less than 2 years of age; some cases were from inadvertent inappropriate use. The report estimated that 1,519 children less than 2 years of age were treated in emergency departments during 2004 to 2005 for adverse events related to cough and cold medications. In October 2007, the FDA Nonprescription Drug Advisory Committee and the Pediatric Advisory Committee recommended that nonprescription cough and cold products containing pseudoephedrine, dextromethorphan, chlorpheniramine, diphenhydramine, brompheniramine, phenylephrine, clemastine, or guaifenesin not be used in children less than 6 years of age. In January 2008, the FDA issued a Public Health Advisory recommending that OTC cough and cold products not be used in infants and children less than 2 years. The FDA recommends that if these products are used in children greater than 2 years, labels should be read carefully, caution should be used when administering multiple products, and only measuring devices specifically designed for use with medications should be used. Clinicians should thoroughly assess each patient's use of similar products, both prescription and nonprescription, to avoid duplication of therapy and the potential for inadvertent overdose.

Labor, obstetric delivery, pregnancy

Chlorpheniramine; phenylephrine in classified as FDA pregnancy risk category C. It is generally recommended to avoid systemic phenylephrine during pregnancy due to the potential vasoconstrictive effects. Systemic phenylephrine must be used only when the benefit to the mother outweighs the risk to the fetus during late pregnancy, labor or obstetric delivery; when used during this time phenylephrine can cause fetal anoxia and/or bradycardia due to increased uterine contractility or decreased uterine blood flow. H1-antagonists (such as chlorpheniramine) are not recommended for use in the last 2 weeks of pregnancy due to a possible association between these drugs and retrolental fibroplasia in premature neonates. Chlorpheniramine; phenylephrine should only be used in pregnancy if the potential benefits are greater than the risks, and use should be limited to short-term, 'as needed' administration under the supervision of a qualified health care professional. Non-pharmacologic methods (e.g., fluids and rest) are recommended to be tried first for symptomatic relief of colds or allergies during pregnancy.

Breast-feeding

Chlorpheniramine; phenylephrine is contraindicated during breast-feeding. The effects of chlorpheniramine or phenylephrine in nursing infants is unknown but may manifest as irritability, disturbed sleeping patterns, drowsiness, hyperexcitability, or excessive crying. Alternative methods of feeding should be used if routine therapy is necessary in the breast-feeding mother.

Bladder obstruction, prostatic hypertrophy, urinary retention

Chlorpheniramine; phenylephrine may cause a variety of adverse genitourinary effects. Chlorpheniramine; phenylephrine may exacerbate urinary retention and is contraindicated in patients with this symptomatology. Due to the anticholinergic effects of chlorpheniramine, a worsening of symptoms may occur in patients with bladder obstruction and benign prostatic hypertrophy.

Anticholinergic medications, geriatric

Caution is advised when using chlorpheniramine in geriatric adults because they may be more sensitive to the anticholinergic effects of chlorpheniramine than younger adults. The anticholinergic effects of chlorpheniramine may be significant and are additive with other anticholinergic medications, particularly

in the elderly. Elderly patients are also more likely to experience adverse effects from sympathomimetic amines, such as phenylephrine. According to the Beers Criteria, first-generation sedating antihistamines are considered potentially inappropriate medications (PIMs) in elderly patients; avoid use as they are highly anticholinergic, there is reduced clearance in advanced age, tolerance develops when used as hypnotics, and there is a greater risk of anticholinergic effects (e.g., confusion, dry mouth, constipation) and toxicity compared to younger adults. Avoid drugs with strong anticholinergic properties in geriatric patients with the following conditions due to the potential for exacerbation of the condition or adverse effects: dementia/cognitive impairment (adverse CNS effects), delirium/high risk of delirium (possible new-onset or worsening delirium), or lower urinary tract symptoms/benign prostatic hyperplasia in men (urinary retention or hesitancy).[63923] The federal Omnibus Budget Reconciliation Act (OBRA) regulates medication use in residents of long-term care facilities; cough, cold, and allergy medications should be used only for a limited duration (less than 14 days) unless there is documented evidence of enduring symptoms that cannot otherwise be alleviated. First-generation antihistamines, such as chlorpheniramine, have strong anticholinergic properties and are not considered medications of choice in older individuals. Oral decongestants, such as phenylephrine, should be used cautiously in patients who have insomnia or hypertension.[60742]

Constipation, GI disease, GI obstruction, ileus, peptic ulcer disease, pyloric stenosis, ulcerative colitis

Antihistamines, such as chlorpheniramine, can reduce GI motility. Chlorpheniramine; phenylephrine should be avoided if possible in patients with GI disease including GI obstruction or ileus, ulcerative colitis, or pre-existing constipation. Due to the anticholinergic effects of chlorpheniramine, a worsening of symptoms may occur in patients with pyloric stenosis or stenosing peptic ulcer disease.

Closed-angle glaucoma, contact lenses, increased intraocular pressure

Chlorpheniramine; phenylephrine is contraindicated in patients with closed-angle glaucoma. Increased intraocular pressure may occur from the anticholinergic actions of chlorpheniramine and/or sympathomimetic actions of phenylephrine, precipitating an acute attack of glaucoma. Elderly patients are more susceptible to these effects, including possible precipitation of undiagnosed glaucoma. Ocular effects resulting from the anticholinergic effects of chlorpheniramine also include dry eyes or blurred vision. This may be of significance in the elderly and wearers of contact lenses.

Diabetes mellitus, hyperthyroidism, peripheral vascular disease, thyrotoxicosis

The sympathomimetic actions of phenylephrine can exacerbate diabetes mellitus, peripheral vascular disease, and hyperthyroidism (including thyrotoxicosis). Chlorpheniramine; phenylephrine should be used with caution in patients with these conditions.

MAOI therapy

Chlorpheniramine; phenylephrine use is contraindicated concurrently or within two weeks of MAOI therapy.

3.2 ADVERSE REACTIONS

Severe

stroke / Early / Incidence not known
arrhythmia exacerbation / Early / Incidence not known
hypertensive crisis / Early / Incidence not known
myocardial infarction / Delayed / Incidence not known

Moderate

hypotension / Rapid / Incidence not known
premature ventricular contractions (PVCs) / Early / Incidence not known

angina / Early / Incidence not known
sinus tachycardia / Rapid / Incidence not known
hypertension / Early / Incidence not known
supraventricular tachycardia (SVT) / Early / Incidence not known

DRUG 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: (Minor) Close monitoring of blood pressure or the selection of alternative therapeutic agents to the sympathomimetic agent may be needed in patients receiving a beta-blocker. Sympathomimetics, such as amphetamines, phentermine, and decongestants (e.g., pseudoephedrine, phenylephrine), and many other drugs, may increase both systolic and diastolic blood pressure and may counteract the activity of the beta-blockers. Concurrent use increases the risk of unopposed alpha-adrenergic activity. Increased blood pressure, bradycardia, or heart block may occur due to excessive alpha-adrenergic receptor stimulation.
Acetaminophen; Aspirin, ASA; Caffeine: (Moderate) CNS-stimulating actions of caffeine can be additive with other CNS stimulants or psychostimulants like phenylephrine; caffeine should be avoided or used cautiously. 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.
Acetaminophen; Butalbital: (Moderate) Additive CNS depression may occur if barbiturates are co-used with sedating antihistamines, such as chlorpheniramine. Monitor for additive CNS and respiratory effects, and warn about the potential effects to driving and other activities.
Acetaminophen; Butalbital; Caffeine: (Moderate) Additive CNS depression may occur if barbiturates are co-used with sedating antihistamines, such as chlorpheniramine. Monitor for additive CNS and respiratory effects, and warn about the potential effects to driving and other activities. (Moderate) CNS-stimulating actions of caffeine can be additive with other CNS stimulants or psychostimulants like phenylephrine; caffeine should be avoided or used cautiously. 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.
Acetaminophen; Butalbital; Caffeine; Codeine: (Moderate) Additive CNS depression may occur if barbiturates are co-used with sedating antihistamines, such as chlorpheniramine. Monitor for additive CNS and respiratory effects, and warn about the potential effects to driving and other activities. (Moderate) CNS-stimulating actions of caffeine can be additive with other CNS stimulants or psychostimulants like phenylephrine; caffeine should be avoided or used cautiously. 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. (Moderate) Concomitant use of opioid agonists with chlorpheniramine may cause excessive sedation and somnolence. Limit the use of opioid pain medication with chlorpheniramine to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect.

Acetaminophen; Caffeine: (Moderate) CNS-stimulating actions of caffeine can be additive with other CNS stimulants or psychostimulants like phenylephrine; caffeine should be avoided or used cautiously. 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.
Acetaminophen; Caffeine; Dihydrocodeine: (Moderate) CNS-stimulating actions of caffeine can be additive with other CNS stimulants or psychostimulants like phenylephrine; caffeine should be avoided or used cautiously. 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. (Moderate) Concomitant use of opioid agonists with chlorpheniramine may cause excessive sedation and somnolence. Limit the use of opioid pain medication with chlorpheniramine to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect.
Acetaminophen; Caffeine; Magnesium Salicylate; Phenyltoloxamine: (Moderate) CNS-stimulating actions of caffeine can be additive with other CNS stimulants or psychostimulants like phenylephrine; caffeine should be avoided or used cautiously. 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.
Acetaminophen; Caffeine; Phenyltoloxamine; Salicylamide: (Moderate) CNS-stimulating actions of caffeine can be additive with other CNS stimulants or psychostimulants like phenylephrine; caffeine should be avoided or used cautiously. 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.
Acetaminophen; Chlorpheniramine; Dextromethorphan; Pseudoephedrine: (Major) Pseudoephedrine can potentiate the effects and increase the toxicity of other sympathomimetics by adding to their sympathomimetic activity. Although no data are available, pseudoephedrine should be used cautiously in patients using significant quantities of other sympathomimetics.
Acetaminophen; Codeine: (Moderate) Concomitant use of opioid agonists with chlorpheniramine may cause excessive sedation and somnolence. Limit the use of opioid pain medication with chlorpheniramine to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect.
Acetaminophen; Dextromethorphan; Pseudoephedrine: (Major) Pseudoephedrine can potentiate the effects and increase the toxicity of other sympathomimetics by adding to their sympathomimetic activity. Although no data are available, pseudoephedrine should be used cautiously in patients using significant quantities of other sympathomimetics.
Acetaminophen; Dichloralphenazone; Isometheptene: (Moderate) Additive CNS depression may occur if dichloralphenazone is used concomitantly with any of the sedating H1 blockers. Use caution with this combination. Dosage reduction of one or both agents may be necessary.
Acetaminophen; Hydrocodone: (Moderate) Concomitant use of opioid agonists with chlorpheniramine may cause excessive sedation and somnolence. Limit the use of opioid pain medication with chlorpheniramine to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect.
Acetaminophen; Oxycodone: (Moderate) Concomitant use of opioid agonists with chlorpheniramine may cause excessive sedation and somnolence. Limit the use of opioid pain medication with chlorpheniramine to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect.

Acetaminophen; Pentazocine: (Moderate) Use pentazocine with caution in any patient receiving medication with CNS depressant and/or anticholinergic activity. Coadministration of pentazocine with sedating H1-blockers may result in additive respiratory and CNS depression and anticholinergic effects, such as urinary retention and constipation.
Acetaminophen; Propoxyphene: (Moderate) Concomitant use of opioid agonists with chlorpheniramine may cause excessive sedation and somnolence. Limit the use of opioid pain medication with chlorpheniramine to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect.
Acetaminophen; Pseudoephedrine: (Major) Pseudoephedrine can potentiate the effects and increase the toxicity of other sympathomimetics by adding to their sympathomimetic activity. Although no data are available, pseudoephedrine should be used cautiously in patients using significant quantities of other sympathomimetics.
Acetaminophen; Tramadol: (Moderate) Concomitant use of opioid agonists with chlorpheniramine may cause excessive sedation and somnolence. Limit the use of opioid pain medication with chlorpheniramine to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect.
Aclidinium; Formoterol: (Moderate) Caution and close observation should be used when formoterol is used concurrently with other adrenergic sympathomimetics, administered by any route, to avoid potential for increased cardiovascular effects.
Acrivastine; Pseudoephedrine: (Major) Pseudoephedrine can potentiate the effects and increase the toxicity of other sympathomimetics by adding to their sympathomimetic activity. Although no data are available, pseudoephedrine should be used cautiously in patients using significant quantities of other sympathomimetics.
Albiglutide: (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.
Albuterol: (Moderate) Caution and close observation should be used when albuterol is used concurrently with other adrenergic sympathomimetics, administered by any route, to avoid potential for increased cardiovascular effects.
Albuterol; Ipratropium: (Moderate) Caution and close observation should be used when albuterol is used concurrently with other adrenergic sympathomimetics, administered by any route, to avoid potential for increased cardiovascular effects.
Alfentanil: (Moderate) Concomitant use of opioid agonists with chlorpheniramine may cause excessive sedation and somnolence. Limit the use of opioid pain medication with chlorpheniramine to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect.
Aliskiren; Amlodipine: (Moderate) Phenylephrine's cardiovascular effects may reduce the antihypertensive effects of calcium-channel blockers. Well-controlled hypertensive patients receiving decongestant sympathomimetics at recommended doses do not appear to be at high risk for significant elevations in blood pressure; however, increased blood pressure (especially systolic hypertension) has been

reported in some patients.
Aliskiren; Amlodipine; Hydrochlorothiazide, HCTZ: (Moderate) Phenylephrine's cardiovascular effects may reduce the antihypertensive effects of calcium-channel blockers. Well-controlled hypertensive patients receiving decongestant sympathomimetics at recommended doses do not appear to be at high risk for significant elevations in blood pressure; however, increased blood pressure (especially systolic hypertension) has been reported in some patients. (Moderate) The cardiovascular effects of sympathomimetics may reduce the antihypertensive effects produced by diuretics. Well-controlled hypertensive patients receiving decongestant sympathomimetics at recommended doses do not appear at high risk for significant elevations in blood pressure, however, increased blood pressure has been reported in some patients.
Aliskiren; Hydrochlorothiazide, HCTZ: (Moderate) The cardiovascular effects of sympathomimetics may reduce the antihypertensive effects produced by diuretics. Well-controlled hypertensive patients receiving decongestant sympathomimetics at recommended doses do not appear at high risk for significant elevations in blood pressure, however, increased blood pressure has been reported in some patients.
Alogliptin; Metformin: (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.
Alogliptin; Pioglitazone: (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.
Alosetron: (Moderate) Alosetron, if combined with drugs that possess anticholinergic properties like sedating H1 blockers, may seriously worsen constipation, leading to events such as GI obstruction/impaction or paralytic ileus.
Alpha-blockers: (Major) Sympathomimetics can antagonize the effects of antihypertensives such as alpha-blockers when administered concomitantly.
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.
Alprazolam: (Moderate) The therapeutic effect of phenylephrine may be decreased in patients receiving benzodiazepines. Monitor patients for decreased pressor effect if these agents are administered concomitantly.

Amantadine: (Moderate) Medications with significant anticholinergic activity may potentiate the anticholinergic effects of amantadine, and may increase the risk of antimuscarinic-related side effects. Additive drowsiness may also occur.
Ambenonium Chloride: (Moderate) The therapeutic benefits of ambenonium may be diminished when coadministered with drugs known to exhibit anticholinergic properties including sedating H1-blockers. When concurrent use cannot be avoided, monitor the patient for reduced ambenonium efficacy.
Ambrisentan: (Major) Sympathomimetics can antagonize the effects of vasodilators when administered concomitantly. Patients should be monitored for reduced efficacy if taking ambrisentan with a sympathomimetic.
Amikacin: (Minor) Chlorpheniramine may effectively mask vestibular symptoms (e.g. dizziness, tinnitus, or vertigo) that are associated with ototoxicity induced by aminoglycosides. Antiemetics block the histamine or acetylcholine response that causes nausea due to vestibular emetic stimuli such as motion.
Amiloride: (Moderate) The cardiovascular effects of sympathomimetics may reduce the antihypertensive effects produced by diuretics. Well-controlled hypertensive patients receiving decongestant sympathomimetics at recommended doses do not appear at high risk for significant elevations in blood pressure, however, increased blood pressure has been reported in some patients.
Amiloride; Hydrochlorothiazide, HCTZ: (Moderate) The cardiovascular effects of sympathomimetics may reduce the antihypertensive effects produced by diuretics. Well-controlled hypertensive patients receiving decongestant sympathomimetics at recommended doses do not appear at high risk for significant elevations in blood pressure, however, increased blood pressure has been reported in some patients.
Aminoglycosides: (Minor) Chlorpheniramine may effectively mask vestibular symptoms (e.g. dizziness, tinnitus, or vertigo) that are associated with ototoxicity induced by aminoglycosides. Antiemetics block the histamine or acetylcholine response that causes nausea due to vestibular emetic stimuli such as motion.
Amiodarone: (Moderate) Use phenylephrine with caution in patients receiving amiodarone. Amiodarone possesses alpha-adrenergic blocking properties and can directly counteract the effects of phenylephrine. Phenylephrine also can block the effects of amiodarone. Monitor patients for decreased pressor effect and decreased amiodarone activity if these agents are administered concomitantly.
Amitriptyline; Chlordiazepoxide: (Moderate) The therapeutic effect of phenylephrine may be decreased in patients receiving benzodiazepines. Monitor patients for decreased pressor effect if these agents are administered concomitantly.
Amlodipine: (Moderate) Phenylephrine's cardiovascular effects may reduce the antihypertensive effects of calcium-channel blockers. Well-controlled hypertensive patients receiving decongestant sympathomimetics at recommended doses do not appear to be at high risk for significant elevations in blood pressure; however, increased blood pressure (especially systolic hypertension) has been reported in some patients.
Amlodipine; Atorvastatin: (Moderate) Phenylephrine's cardiovascular effects may reduce the antihypertensive effects of calcium-channel blockers. Well-controlled hypertensive patients receiving decongestant sympathomimetics at recommended doses do not appear to be at high risk for significant elevations in blood pressure; however, increased blood pressure (especially systolic hypertension) has been reported in some patients.
Amlodipine; Benazepril: (Moderate) Phenylephrine's cardiovascular effects may reduce the antihypertensive effects of calcium-channel blockers. Well-controlled hypertensive patients receiving decongestant sympathomimetics at recommended doses do not appear to be at high risk for significant elevations in blood pressure; however, increased blood pressure (especially systolic hypertension) has been reported in some patients.
Amlodipine; Celecoxib: (Moderate) A dosage adjustment may be warranted for chlorpheniramine if

coadministered with celecoxib due to the potential for celecoxib to enhance the exposure and toxicity of chlorpheniramine. Celecoxib is a CYP2D6 inhibitor, and chlorpheniramine is a CYP2D6 substrate. (Moderate) Phenylephrine's cardiovascular effects may reduce the antihypertensive effects of calcium-channel blockers. Well-controlled hypertensive patients receiving decongestant sympathomimetics at recommended doses do not appear to be at high risk for significant elevations in blood pressure; however, increased blood pressure (especially systolic hypertension) has been reported in some patients.
Amlodipine; Hydrochlorothiazide, HCTZ; Olmesartan: (Moderate) Phenylephrine's cardiovascular effects may reduce the antihypertensive effects of calcium-channel blockers. Well-controlled hypertensive patients receiving decongestant sympathomimetics at recommended doses do not appear to be at high risk for significant elevations in blood pressure; however, increased blood pressure (especially systolic hypertension) has been reported in some patients. (Moderate) The cardiovascular effects of sympathomimetics may reduce the antihypertensive effects produced by diuretics. Well-controlled hypertensive patients receiving decongestant sympathomimetics at recommended doses do not appear at high risk for significant elevations in blood pressure, however, increased blood pressure has been reported in some patients.
Amlodipine; Hydrochlorothiazide, HCTZ; Valsartan: (Moderate) Phenylephrine's cardiovascular effects may reduce the antihypertensive effects of calcium-channel blockers. Well-controlled hypertensive patients receiving decongestant sympathomimetics at recommended doses do not appear to be at high risk for significant elevations in blood pressure; however, increased blood pressure (especially systolic hypertension) has been reported in some patients. (Moderate) The cardiovascular effects of sympathomimetics may reduce the antihypertensive effects produced by diuretics. Well-controlled hypertensive patients receiving decongestant sympathomimetics at recommended doses do not appear at high risk for significant elevations in blood pressure, however, increased blood pressure has been reported in some patients.
Amlodipine; Olmesartan: (Moderate) Phenylephrine's cardiovascular effects may reduce the antihypertensive effects of calcium-channel blockers. Well-controlled hypertensive patients receiving decongestant sympathomimetics at recommended doses do not appear to be at high risk for significant elevations in blood pressure; however, increased blood pressure (especially systolic hypertension) has been reported in some patients.
Amlodipine; Telmisartan: (Moderate) Phenylephrine's cardiovascular effects may reduce the antihypertensive effects of calcium-channel blockers. Well-controlled hypertensive patients receiving decongestant sympathomimetics at recommended doses do not appear to be at high risk for significant elevations in blood pressure; however, increased blood pressure (especially systolic hypertension) has been reported in some patients.
Amlodipine; Valsartan: (Moderate) Phenylephrine's cardiovascular effects may reduce the antihypertensive effects of calcium-channel blockers. Well-controlled hypertensive patients receiving decongestant sympathomimetics at recommended doses do not appear to be at high risk for significant elevations in blood pressure; however, increased blood pressure (especially systolic hypertension) has been reported in some patients.
Amobarbital: (Moderate) Additive CNS depression may occur if barbiturates are co-used with sedating antihistamines, such as chlorpheniramine. Monitor for additive CNS and respiratory effects, and warn about the potential effects to driving and other activities.
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 direct-acting sympathomimetics, but decrease the pressor response to indirect-acting sympathomimetics, however, the

data are not consistent. (Moderate) Additive anticholinergic effects may be seen when amoxapine is used concomitantly with drugs are known to possess relatively significant antimuscarinic properties, including sedating H1-blockers. Antimuscarinic effects might be seen not only on GI smooth muscle, but also on bladder function, the eye, and temperature Additive sedation may also occur.

Amphetamine: (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.

Amphetamine; Dextroamphetamine Salts: (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.

Amphetamine; Dextroamphetamine: (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.

Angiotensin II receptor antagonists: (Moderate) The cardiovascular effects of sympathomimetics may reduce the antihypertensive effects produced by angiotensin II receptor antagonists. Well-controlled hypertensive patients receiving phenylephrine at recommended doses do not appear at high risk for significant elevations in blood pressure; however, increased blood pressure (especially systolic hypertension) has been reported in some patients.

Angiotensin-converting enzyme inhibitors: (Moderate) The cardiovascular effects of sympathomimetics may reduce the antihypertensive effects produced by angiotensin-converting enzyme inhibitors. Well-controlled hypertensive patients receiving phenylephrine at recommended doses do not appear at high risk for significant elevations in blood pressure, however, increased blood pressure (especially systolic hypertension) has been reported in some patients.

Anticholinergics: (Moderate) The anticholinergic effects of sedating H1-blockers may be enhanced when combined with other antimuscarinics. Clinicians should note that anticholinergic effects might be seen not only on GI smooth muscle, but also on bladder function, the eye, and temperature regulation. Additive drowsiness may also occur when antimuscarinics are combined with sedating antihistamines.

Apomorphine: (Moderate) Apomorphine causes significant somnolence. Concomitant administration of apomorphine and chlorpheniramine could result in additive depressant effects. Careful monitoring is recommended during combined use. A dose reduction of one or both drugs may be warranted.

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.

Artemether; Lumefantrine: (Moderate) Lumefantrine is an inhibitor and chlorpheniramine is a substrate/inhibitor of the CYP2D6 isoenzyme; therefore, coadministration may lead to increased chlorpheniramine concentrations. Concomitant use warrants caution due to the potential for increased side effects.

Articaine; Epinephrine: (Major) Because epinephrine is a sympathomimetic drug with agonist actions at both the alpha and beta receptors, caution is warranted in patients receiving epinephrine concomitantly with other sympathomimetics as additive pharmacodynamic effects are possible, some which may be

undesirable.
Asenapine: (Moderate) Using drugs that can cause CNS depression, such as sedating H1-blockers, concomitantly with asenapine may increase both the frequency and the intensity of adverse effects such as drowsiness, sedation, and dizziness.
Aspirin, ASA; Butalbital; Caffeine: (Moderate) Additive CNS depression may occur if barbiturates are co-used with sedating antihistamines, such as chlorpheniramine. Monitor for additive CNS and respiratory effects, and warn about the potential effects to driving and other activities. (Moderate) CNS-stimulating actions of caffeine can be additive with other CNS stimulants or psychostimulants like phenylephrine; caffeine should be avoided or used cautiously. 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.
Aspirin, ASA; Butalbital; Caffeine; Codeine: (Moderate) Additive CNS depression may occur if barbiturates are co-used with sedating antihistamines, such as chlorpheniramine. Monitor for additive CNS and respiratory effects, and warn about the potential effects to driving and other activities. (Moderate) CNS-stimulating actions of caffeine can be additive with other CNS stimulants or psychostimulants like phenylephrine; caffeine should be avoided or used cautiously. 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. (Moderate) Concomitant use of opioid agonists with chlorpheniramine may cause excessive sedation and somnolence. Limit the use of opioid pain medication with chlorpheniramine to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect.
Aspirin, ASA; Caffeine; Dihydrocodeine: (Moderate) CNS-stimulating actions of caffeine can be additive with other CNS stimulants or psychostimulants like phenylephrine; caffeine should be avoided or used cautiously. 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. (Moderate) Concomitant use of opioid agonists with chlorpheniramine may cause excessive sedation and somnolence. Limit the use of opioid pain medication with chlorpheniramine to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect.
Aspirin, ASA; Caffeine; Orphenadrine: (Moderate) Additive anticholinergic effects may be seen when drugs with anticholinergic properties, like sedating H1-blockers and orphenadrine, are used concomitantly. Adverse effects may be seen not only on GI smooth muscle, but also on bladder function, the CNS, the eye, and temperature regulation. Additive drowsiness may also occur. (Moderate) CNS-stimulating actions of caffeine can be additive with other CNS stimulants or psychostimulants like phenylephrine; caffeine should be avoided or used cautiously. 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.
Aspirin, ASA; Carisoprodol: (Moderate) Carisoprodol is metabolized to meprobamate, a significant CNS depressant. Carisoprodol can cause additive CNS depression if used concomitantly with other CNS depressants. Additive effects of sedation and dizziness, which can impair the ability to undertake tasks requiring mental alertness, may occur if carisoprodol is taken with sedating H1-blockers. Utilize appropriate caution if carisoprodol is coadministered with another CNS depressant.
Aspirin, ASA; Carisoprodol; Codeine: (Moderate) Carisoprodol is metabolized to meprobamate, a significant CNS depressant. Carisoprodol can cause additive CNS depression if used concomitantly with other CNS depressants. Additive effects of sedation and dizziness, which can impair the ability to

undertake tasks requiring mental alertness, may occur if carisoprodol is taken with sedating H1-blockers. Utilize appropriate caution if carisoprodol is coadministered with another CNS depressant. (Moderate) Concomitant use of opioid agonists with chlorpheniramine may cause excessive sedation and somnolence. Limit the use of opioid pain medication with chlorpheniramine to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect.

Aspirin, ASA; Oxycodone: (Moderate) Concomitant use of opioid agonists with chlorpheniramine may cause excessive sedation and somnolence. Limit the use of opioid pain medication with chlorpheniramine to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect.

Atazanavir; Cobicistat: (Moderate) Caution is warranted when cobicistat is administered with chlorpheniramine as there is a potential for elevated chlorpheniramine and cobicistat concentrations. Chlorpheniramine is a CYP2D6 substrate/inhibitor. Cobicistat is a substrate/inhibitor of CYP2D6.

Atenolol: (Minor) Close monitoring of blood pressure or the selection of alternative therapeutic agents to the sympathomimetic agent may be needed in patients receiving a beta-blocker. Sympathomimetics, such as amphetamines, phentermine, and decongestants (e.g., pseudoephedrine, phenylephrine), and many other drugs, may increase both systolic and diastolic blood pressure and may counteract the activity of the beta-blockers. Concurrent use increases the risk of unopposed alpha-adrenergic activity. Increased blood pressure, bradycardia, or heart block may occur due to excessive alpha-adrenergic receptor stimulation.

Atenolol; Chlorthalidone: (Moderate) The cardiovascular effects of sympathomimetics may reduce the antihypertensive effects produced by diuretics. Well-controlled hypertensive patients receiving decongestant sympathomimetics at recommended doses do not appear at high risk for significant elevations in blood pressure, however, increased blood pressure has been reported in some patients. (Minor) Close monitoring of blood pressure or the selection of alternative therapeutic agents to the sympathomimetic agent may be needed in patients receiving a beta-blocker. Sympathomimetics, such as amphetamines, phentermine, and decongestants (e.g., pseudoephedrine, phenylephrine), and many other drugs, may increase both systolic and diastolic blood pressure and may counteract the activity of the beta-blockers. Concurrent use increases the risk of unopposed alpha-adrenergic activity. Increased blood pressure, bradycardia, or heart block may occur due to excessive alpha-adrenergic receptor stimulation.

Atomoxetine: (Moderate) Due to the potential for additive increases in blood pressure and heart rate, atomoxetine should be used cautiously with vasopressors such as phenylephrine. Consider monitoring the patient's blood pressure and heart rate at baseline and regularly if vasopressors are coadministered with atomoxetine.

Atropine: (Major) Atropine blocks the vagal reflex bradycardia caused by sympathomimetic agents, such as phenylephrine, and increases its pressor effect.

Atropine; Benzoic Acid; Hyoscyamine; Methenamine; Methylene Blue; Phenyl Salicylate: (Major) Atropine blocks the vagal reflex bradycardia caused by sympathomimetic agents, such as phenylephrine, and increases its pressor effect.

Atropine; Difenoxin: (Major) Atropine blocks the vagal reflex bradycardia caused by sympathomimetic agents, such as phenylephrine, and increases its pressor effect. (Moderate) An enhanced CNS depressant effect may occur when diphenoxylate/difenoxin is combined with other CNS depressants. Diphenoxylate/difenoxin decreases GI motility. Other drugs that also decrease GI motility, such as sedating H1 blockers, may produce additive effects with diphenoxylate/difenoxin if used concomitantly.

Atropine; Diphenoxylate: (Major) Atropine blocks the vagal reflex bradycardia caused by sympathomimetic agents, such as phenylephrine, and increases its pressor effect. (Moderate) An enhanced CNS depressant effect may occur when diphenoxylate/difenoxin is combined with other CNS depressants.

Diphenoxylate/difenoxin decreases GI motility. Other drugs that also decrease GI motility, such as sedating H1 blockers, may produce additive effects with diphenoxylate/difenoxin if used concomitantly.
Atropine; Edrophonium: (Major) Atropine blocks the vagal reflex bradycardia caused by sympathomimetic agents, such as phenylephrine, and increases its pressor effect.
Atropine; Hyoscyamine; Phenobarbital; Scopolamine: (Major) Atropine blocks the vagal reflex bradycardia caused by sympathomimetic agents, such as phenylephrine, and increases its pressor effect. (Moderate) Additive CNS depression may occur if barbiturates are co-used with sedating antihistamines, such as chlorpheniramine. Monitor for additive CNS and respiratory effects, and warn about the potential effects to driving and other activities.
Avanafil: (Minor) The therapeutic effect of phenylephrine injection may be decreased in patients receiving phosphodiesterase inhibitors. A decreased pressor effect of phenylephrine might occur. Monitor for proper blood pressure when these drugs are used together,
Azelastine: (Major) An enhanced CNS depressant effect may occur when azelastine is combined with other CNS depressants including sedating H1-blockers; avoid concurrent use.
Azelastine; Fluticasone: (Major) An enhanced CNS depressant effect may occur when azelastine is combined with other CNS depressants including sedating H1-blockers; avoid concurrent use. (Moderate) The therapeutic effect of phenylephrine may be increased in patient receiving corticosteroids, such as hydrocortisone. Monitor patients for increased pressor effect if these agents are administered concomitantly.
Azilsartan; Chlorthalidone: (Moderate) The cardiovascular effects of sympathomimetics may reduce the antihypertensive effects produced by diuretics. Well-controlled hypertensive patients receiving decongestant sympathomimetics at recommended doses do not appear at high risk for significant elevations in blood pressure, however, increased blood pressure has been reported in some patients.
Baclofen: (Moderate) An enhanced CNS depressant effect may occur when sedating H1-blockers are combined with other CNS depressants including skeletal muscle relaxants, such as baclofen.
Barbiturates: (Moderate) Additive CNS depression may occur if barbiturates are co-used with sedating antihistamines, such as chlorpheniramine. Monitor for additive CNS and respiratory effects, and warn about the potential effects to driving and other activities.
Beclomethasone: (Moderate) The therapeutic effect of phenylephrine may be increased in patient receiving corticosteroids, such as hydrocortisone. Monitor patients for increased pressor effect if these agents are administered concomitantly.
Belladonna Alkaloids; Ergotamine; Phenobarbital: (Severe) Ergot alkaloids should not be administered with vasoconstrictors such as vasopressors (e.g., norepinephrine, dopamine, phenylephrine) since combining these agents may produce a synergistic increase in blood pressure. There is also an additive risk of peripheral ischemia or gangrene. Of note, at therapeutic doses, ergoloid mesylates lack the vasoconstrictor properties of the natural ergot alkaloids; therefore, ergoloid mesylates are not expected to interact with sympathomimetics. (Moderate) Additive CNS depression may occur if barbiturates are co-used with sedating antihistamines, such as chlorpheniramine. Monitor for additive CNS and respiratory effects, and warn about the potential effects to driving and other activities.
Belladonna; Opium: (Moderate) Concomitant use of opioid agonists with chlorpheniramine may cause excessive sedation and somnolence. Limit the use of opioid pain medication with chlorpheniramine to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect.
Benazepril; Hydrochlorothiazide, HCTZ: (Moderate) The cardiovascular effects of sympathomimetics may reduce the antihypertensive effects produced by diuretics. Well-controlled hypertensive patients receiving decongestant sympathomimetics at recommended doses do not appear at high risk for significant

elevations in blood pressure, however, increased blood pressure has been reported in some patients.
Bendroflumethiazide; Nadolol: (Moderate) The cardiovascular effects of sympathomimetics may reduce the antihypertensive effects produced by diuretics. Well-controlled hypertensive patients receiving decongestant sympathomimetics at recommended doses do not appear at high risk for significant elevations in blood pressure, however, increased blood pressure has been reported in some patients. (Minor) Close monitoring of blood pressure or the selection of alternative therapeutic agents to the sympathomimetic agent may be needed in patients receiving a beta-blocker. Sympathomimetics, such as amphetamines, phentermine, and decongestants (e.g., pseudoephedrine, phenylephrine), and many other drugs, may increase both systolic and diastolic blood pressure and may counteract the activity of the beta-blockers. Concurrent use increases the risk of unopposed alpha-adrenergic activity. Increased blood pressure, bradycardia, or heart block may occur due to excessive alpha-adrenergic receptor stimulation.
Benzhydrocodone; Acetaminophen: (Moderate) Concomitant use of opioid agonists with chlorpheniramine may cause excessive sedation and somnolence. Limit the use of opioid pain medication with chlorpheniramine to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect.
Benzodiazepines: (Moderate) Coadministration can potentiate the CNS effects (e.g., increased sedation or respiratory depression) of either agent. Use caution with this combination. (Moderate) The therapeutic effect of phenylephrine may be decreased in patients receiving benzodiazepines. Monitor patients for decreased pressor effect if these agents are administered concomitantly.
Benzphetamine: (Moderate) Amphetamines may pharmacodynamically counteract the sedative properties of some antihistamines, such as the sedating H1-blockers. 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.
Beta-blockers: (Minor) Close monitoring of blood pressure or the selection of alternative therapeutic agents to the sympathomimetic agent may be needed in patients receiving a beta-blocker. Sympathomimetics, such as amphetamines, phentermine, and decongestants (e.g., pseudoephedrine, phenylephrine), and many other drugs, may increase both systolic and diastolic blood pressure and may counteract the activity of the beta-blockers. Concurrent use increases the risk of unopposed alpha-adrenergic activity. Increased blood pressure, bradycardia, or heart block may occur due to excessive alpha-adrenergic receptor stimulation.
Betamethasone: (Moderate) The therapeutic effect of phenylephrine may be increased in patient receiving corticosteroids, such as hydrocortisone. Monitor patients for increased pressor effect if these agents are administered concomitantly.
Betaxolol: (Minor) Close monitoring of blood pressure or the selection of alternative therapeutic agents to the sympathomimetic agent may be needed in patients receiving a beta-blocker. Sympathomimetics, such as amphetamines, phentermine, and decongestants (e.g., pseudoephedrine, phenylephrine), and many other drugs, may increase both systolic and diastolic blood pressure and may counteract the activity of the beta-blockers. Concurrent use increases the risk of unopposed alpha-adrenergic activity. Increased blood pressure, bradycardia, or heart block may occur due to excessive alpha-adrenergic receptor stimulation.
Bethanechol: (Moderate) Bethanechol offsets the effects of sympathomimetics at sites where sympathomimetic and cholinergic receptors have opposite effects.
Bisoprolol: (Minor) Close monitoring of blood pressure or the selection of alternative therapeutic agents to the sympathomimetic agent may be needed in patients receiving a beta-blocker. Sympathomimetics, such as amphetamines, phentermine, and decongestants (e.g., pseudoephedrine, phenylephrine), and many

other drugs, may increase both systolic and diastolic blood pressure and may counteract the activity of the beta-blockers. Concurrent use increases the risk of unopposed alpha-adrenergic activity. Increased blood pressure, bradycardia, or heart block may occur due to excessive alpha-adrenergic receptor stimulation.
Bisoprolol; Hydrochlorothiazide, HCTZ: (Moderate) The cardiovascular effects of sympathomimetics may reduce the antihypertensive effects produced by diuretics. Well-controlled hypertensive patients receiving decongestant sympathomimetics at recommended doses do not appear at high risk for significant elevations in blood pressure, however, increased blood pressure has been reported in some patients. (Minor) Close monitoring of blood pressure or the selection of alternative therapeutic agents to the sympathomimetic agent may be needed in patients receiving a beta-blocker. Sympathomimetics, such as amphetamines, phentermine, and decongestants (e.g., pseudoephedrine, phenylephrine), and many other drugs, may increase both systolic and diastolic blood pressure and may counteract the activity of the beta-blockers. Concurrent use increases the risk of unopposed alpha-adrenergic activity. Increased blood pressure, bradycardia, or heart block may occur due to excessive alpha-adrenergic receptor stimulation.
Bosentan: (Major) Avoid use of sympathomimetic agents with bosentan. Sympathomimetics counteract the medications used to stabilize pulmonary hypertension, including bosentan. 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.
Bretylium: (Moderate) Monitor blood pressure closely when sympathomimetics are administered with bretylium. The pressor effects of catecholamines are enhanced by bretylium.
Brimonidine; Timolol: (Minor) Close monitoring of blood pressure or the selection of alternative therapeutic agents to the sympathomimetic agent may be needed in patients receiving a beta-blocker. Sympathomimetics, such as amphetamines, phentermine, and decongestants (e.g., pseudoephedrine, phenylephrine), and many other drugs, may increase both systolic and diastolic blood pressure and may counteract the activity of the beta-blockers. Concurrent use increases the risk of unopposed alpha-adrenergic activity. Increased blood pressure, bradycardia, or heart block may occur due to excessive alpha-adrenergic receptor stimulation.
Bromocriptine: (Moderate) The combination of bromocriptine with phenylephrine may cause headache, tachycardia, other cardiovascular abnormalities, seizures, and other serious effects. Concurrent use of bromocriptine and phenylephrine 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 acetaminophen; dichloralphenazone; isometheptene for a headache. A second case involved a post-partum patient receiving bromocriptine who was later prescribed phenylpropanolamine; guaifenesin and subsequently developed hypertension, tachycardia, seizures, and cerebral vasospasm.
Brompheniramine; Carbetapentane; Phenylephrine: (Moderate) Drowsiness has been reported during administration of carbetapentane. An enhanced CNS depressant effect may occur when carbetapentane is combined with other CNS depressants including sedating h1-blockers.
Brompheniramine; Guaifenesin; Hydrocodone: (Moderate) Concomitant use of opioid agonists with chlorpheniramine may cause excessive sedation and somnolence. Limit the use of opioid pain medication with chlorpheniramine to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect.

Brompheniramine; Hydrocodone; Pseudoephedrine: (Major) Pseudoephedrine can potentiate the effects and increase the toxicity of other sympathomimetics by adding to their sympathomimetic activity. Although no data are available, pseudoephedrine should be used cautiously in patients using significant quantities of other sympathomimetics. (Moderate) Concomitant use of opioid agonists with chlorpheniramine may cause excessive sedation and somnolence. Limit the use of opioid pain medication with chlorpheniramine to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect.
Brompheniramine; Pseudoephedrine: (Major) Pseudoephedrine can potentiate the effects and increase the toxicity of other sympathomimetics by adding to their sympathomimetic activity. Although no data are available, pseudoephedrine should be used cautiously in patients using significant quantities of other sympathomimetics.
Budesonide: (Moderate) The therapeutic effect of phenylephrine may be increased in patient receiving corticosteroids, such as hydrocortisone. Monitor patients for increased pressor effect if these agents are administered concomitantly.
Budesonide; Formoterol: (Moderate) Caution and close observation should be used when formoterol is used concurrently with other adrenergic sympathomimetics, administered by any route, to avoid potential for increased cardiovascular effects. (Moderate) The therapeutic effect of phenylephrine may be increased in patient receiving corticosteroids, such as hydrocortisone. Monitor patients for increased pressor effect if these agents are administered concomitantly.
Budesonide; Glycopyrrolate; Formoterol: (Moderate) Caution and close observation should be used when formoterol is used concurrently with other adrenergic sympathomimetics, administered by any route, to avoid potential for increased cardiovascular effects. (Moderate) The therapeutic effect of phenylephrine may be increased in patient receiving corticosteroids, such as hydrocortisone. Monitor patients for increased pressor effect if these agents are administered concomitantly.
Bumetanide: (Moderate) The cardiovascular effects of sympathomimetics may reduce the antihypertensive effects produced by diuretics. Well-controlled hypertensive patients receiving decongestant sympathomimetics at recommended doses do not appear at high risk for significant elevations in blood pressure, however, increased blood pressure has been reported in some patients.
Buprenorphine: (Moderate) If concurrent use of sedating H1-blockers and buprenorphine is necessary, consider a dose reduction of one or both drugs because of the potential for additive pharmacological effects. Hypotension, profound sedation, coma, respiratory depression, or death may occur during co-administration of buprenorphine and other CNS depressants. Prior to concurrent use of buprenorphine in patients taking a CNS depressant, assess the level of tolerance to CNS depression that has developed, the duration of use, and the patient's overall response to treatment. Evaluate the patient's use of alcohol or illicit drugs. It is recommended that the injectable buprenorphine dose be halved for patients who receive other drugs with CNS depressant effects; for the buprenorphine transdermal patch, start with the 5 mcg/hour patch. Monitor patients for sedation or respiratory depression.
Buprenorphine; Naloxone: (Moderate) If concurrent use of sedating H1-blockers and buprenorphine is necessary, consider a dose reduction of one or both drugs because of the potential for additive pharmacological effects. Hypotension, profound sedation, coma, respiratory depression, or death may occur during co-administration of buprenorphine and other CNS depressants. Prior to concurrent use of buprenorphine in patients taking a CNS depressant, assess the level of tolerance to CNS depression that has developed, the duration of use, and the patient's overall response to treatment. Evaluate the patient's use of alcohol or illicit drugs. It is recommended that the injectable buprenorphine dose be halved for patients who receive other drugs with CNS depressant effects; for the buprenorphine transdermal patch,

start with the 5 mcg/hour patch. Monitor patients for sedation or respiratory depression.
Buspirone: (Moderate) The combination of buspirone and other CNS depressants, such as the sedating H1-blockers (sedating antihistamines), may increase the risk for sedation.
Butabarbital: (Moderate) Additive CNS depression may occur if barbiturates are co-used with sedating antihistamines, such as chlorpheniramine. Monitor for additive CNS and respiratory effects, and warn about the potential effects to driving and other activities.
Butorphanol: (Moderate) Concomitant use of butorphanol with sedating H1-blockers can potentiate the effects of butorphanol on CNS and/or respiratory depression. Use together with caution. If a CNS depressant needs to be used with butorphanol, use the smallest effective dose and the longest dosing frequency of butorphanol. (Moderate) The rate of butorphanol absorption through the nasal mucosa is decreased when administered with sympathomimetic nasal decongestants such as phenylephrine. However, the extent of absorption is not decreased. A slower onset of action should be expected if butorphanol is administered concurrently with or immediately following a sympathomimetic nasal decongestant.
Caffeine: (Moderate) Caffeine is a CNS-stimulant and such actions are expected to be additive when coadministered with other CNS stimulants or psychostimulants. (Moderate) CNS-stimulating actions of caffeine can be additive with other CNS stimulants or psychostimulants like phenylephrine; caffeine should be avoided or used cautiously. 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; Ergotamine: (Severe) Ergot alkaloids should not be administered with vasoconstrictors such as vasopressors (e.g., norepinephrine, dopamine, phenylephrine) since combining these agents may produce a synergistic increase in blood pressure. There is also an additive risk of peripheral ischemia or gangrene. Of note, at therapeutic doses, ergoloid mesylates lack the vasoconstrictor properties of the natural ergot alkaloids; therefore, ergoloid mesylates are not expected to interact with sympathomimetics. (Moderate) CNS-stimulating actions of caffeine can be additive with other CNS stimulants or psychostimulants like phenylephrine; caffeine should be avoided or used cautiously. 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.
Calcium-channel blockers: (Moderate) Phenylephrine's cardiovascular effects may reduce the antihypertensive effects of calcium-channel blockers. Well-controlled hypertensive patients receiving decongestant sympathomimetics at recommended doses do not appear to be at high risk for significant elevations in blood pressure; however, increased blood pressure (especially systolic hypertension) has been reported in some patients.
Canagliflozin: (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.
Canagliflozin; Metformin: (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.

Candesartan; Hydrochlorothiazide, HCTZ: (Moderate) The cardiovascular effects of sympathomimetics may reduce the antihypertensive effects produced by diuretics. Well-controlled hypertensive patients receiving decongestant sympathomimetics at recommended doses do not appear at high risk for significant elevations in blood pressure, however, increased blood pressure has been reported in some patients.

Cannabidiol: (Moderate) Monitor for excessive sedation and somnolence during coadministration of cannabidiol and sedating H1-blockers. CNS depressants can potentiate the effects of cannabidiol.

Capsaicin; Metaxalone: (Moderate) Concomitant administration of metaxalone with other CNS depressants can potentiate the sedative effects of either agent.

Captopril; Hydrochlorothiazide, HCTZ: (Moderate) The cardiovascular effects of sympathomimetics may reduce the antihypertensive effects produced by diuretics. Well-controlled hypertensive patients receiving decongestant sympathomimetics at recommended doses do not appear at high risk for significant elevations in blood pressure, however, increased blood pressure has been reported in some patients.

Carbetapentane; Chlorpheniramine: (Moderate) Drowsiness has been reported during administration of carbetapentane. An enhanced CNS depressant effect may occur when carbetapentane is combined with other CNS depressants including sedating h1-blockers.

Carbetapentane; Chlorpheniramine; Phenylephrine: (Moderate) Drowsiness has been reported during administration of carbetapentane. An enhanced CNS depressant effect may occur when carbetapentane is combined with other CNS depressants including sedating h1-blockers.

Carbetapentane; Diphenhydramine; Phenylephrine: (Moderate) Drowsiness has been reported during administration of carbetapentane. An enhanced CNS depressant effect may occur when carbetapentane is combined with other CNS depressants including sedating h1-blockers.

Carbetapentane; Guaifenesin: (Moderate) Drowsiness has been reported during administration of carbetapentane. An enhanced CNS depressant effect may occur when carbetapentane is combined with other CNS depressants including sedating h1-blockers.

Carbetapentane; Guaifenesin; Phenylephrine: (Moderate) Drowsiness has been reported during administration of carbetapentane. An enhanced CNS depressant effect may occur when carbetapentane is combined with other CNS depressants including sedating h1-blockers.

Carbetapentane; Phenylephrine: (Moderate) Drowsiness has been reported during administration of carbetapentane. An enhanced CNS depressant effect may occur when carbetapentane is combined with other CNS depressants including sedating h1-blockers.

Carbetapentane; Phenylephrine; Pyrilamine: (Moderate) Drowsiness has been reported during administration of carbetapentane. An enhanced CNS depressant effect may occur when carbetapentane is combined with other CNS depressants including sedating h1-blockers.

Carbetapentane; Pseudoephedrine: (Major) Pseudoephedrine can potentiate the effects and increase the toxicity of other sympathomimetics by adding to their sympathomimetic activity. Although no data are available, pseudoephedrine should be used cautiously in patients using significant quantities of other sympathomimetics. (Moderate) Drowsiness has been reported during administration of carbetapentane. An enhanced CNS depressant effect may occur when carbetapentane is combined with other CNS depressants including sedating h1-blockers.

Carbetapentane; Pyrilamine: (Moderate) Drowsiness has been reported during administration of carbetapentane. An enhanced CNS depressant effect may occur when carbetapentane is combined with other CNS depressants including sedating h1-blockers.

Carbidopa; Levodopa; Entacapone: (Moderate) COMT inhibitors should be given cautiously with other agents that cause CNS depression, including sedating H1-blockers, due to the possibility of additive sedation. COMT inhibitors have also been associated with sudden sleep onset during activities of daily living such as driving, which has resulted in accidents in some cases. Prescribers should re-assess patients for drowsiness or sleepiness regularly throughout treatment, especially since events may occur well after the start of treatment. Patients should be advised to avoid driving or other tasks requiring mental alertness until they know how the combination affects them.
Carbinoxamine; Dextromethorphan; Pseudoephedrine: (Major) Pseudoephedrine can potentiate the effects and increase the toxicity of other sympathomimetics by adding to their sympathomimetic activity. Although no data are available, pseudoephedrine should be used cautiously in patients using significant quantities of other sympathomimetics.
Carbinoxamine; Hydrocodone; Phenylephrine: (Moderate) Concomitant use of opioid agonists with chlorpheniramine may cause excessive sedation and somnolence. Limit the use of opioid pain medication with chlorpheniramine to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect.
Carbinoxamine; Hydrocodone; Pseudoephedrine: (Major) Pseudoephedrine can potentiate the effects and increase the toxicity of other sympathomimetics by adding to their sympathomimetic activity. Although no data are available, pseudoephedrine should be used cautiously in patients using significant quantities of other sympathomimetics. (Moderate) Concomitant use of opioid agonists with chlorpheniramine may cause excessive sedation and somnolence. Limit the use of opioid pain medication with chlorpheniramine to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect.
Carbinoxamine; Pseudoephedrine: (Major) Pseudoephedrine can potentiate the effects and increase the toxicity of other sympathomimetics by adding to their sympathomimetic activity. Although no data are available, pseudoephedrine should be used cautiously in patients using significant quantities of other sympathomimetics.
Cardiac glycosides: (Major) Concomitant use of cardiac glycosides with sympathomimetics can cause arrhythmias because sympathomimetics enhance ectopic pacemaker activity. Caution is warranted during co-administration of digoxin and sympathomimetics.
Carisoprodol: (Moderate) Carisoprodol is metabolized to meprobamate, a significant CNS depressant. Carisoprodol can cause additive CNS depression if used concomitantly with other CNS depressants. Additive effects of sedation and dizziness, which can impair the ability to undertake tasks requiring mental alertness, may occur if carisoprodol is taken with sedating H1-blockers. Utilize appropriate caution if carisoprodol is coadministered with another CNS depressant.
Carteolol: (Minor) Close monitoring of blood pressure or the selection of alternative therapeutic agents to the sympathomimetic agent may be needed in patients receiving a beta-blocker. Sympathomimetics, such as amphetamines, phentermine, and decongestants (e.g., pseudoephedrine, phenylephrine), and many other drugs, may increase both systolic and diastolic blood pressure and may counteract the activity of the beta-blockers. Concurrent use increases the risk of unopposed alpha-adrenergic activity. Increased blood pressure, bradycardia, or heart block may occur due to excessive alpha-adrenergic receptor stimulation.
Carvedilol: (Minor) Close monitoring of blood pressure or the selection of alternative therapeutic agents to the sympathomimetic agent may be needed in patients receiving a beta-blocker. Sympathomimetics, such as amphetamines, phentermine, and decongestants (e.g., pseudoephedrine, phenylephrine), and many other drugs, may increase both systolic and diastolic blood pressure and may counteract the activity of the

beta-blockers. Concurrent use increases the risk of unopposed alpha-adrenergic activity. Increased blood pressure, bradycardia, or heart block may occur due to excessive alpha-adrenergic receptor stimulation.
Celecoxib: (Moderate) A dosage adjustment may be warranted for chlorpheniramine if coadministered with celecoxib due to the potential for celecoxib to enhance the exposure and toxicity of chlorpheniramine. Celecoxib is a CYP2D6 inhibitor, and chlorpheniramine is a CYP2D6 substrate.
Cenobamate: (Moderate) Monitor for excessive sedation and somnolence during coadministration of cenobamate and sedating H1-blockers. Concurrent use may result in additive CNS depression.
Cetirizine: (Moderate) Due to the duplicative and additive pharmacology, concurrent use of cetirizine/levocetirizine with sedating H1-blockers should generally be avoided. Coadministration may increase the risk of anticholinergic and CNS depressant-related side effects. If concurrent use is necessary, monitor for excessive anticholinergic effects, sedation, and somnolence.
Cetirizine; Pseudoephedrine: (Major) Pseudoephedrine can potentiate the effects and increase the toxicity of other sympathomimetics by adding to their sympathomimetic activity. Although no data are available, pseudoephedrine should be used cautiously in patients using significant quantities of other sympathomimetics. (Moderate) Due to the duplicative and additive pharmacology, concurrent use of cetirizine/levocetirizine with sedating H1-blockers should generally be avoided. Coadministration may increase the risk of anticholinergic and CNS depressant-related side effects. If concurrent use is necessary, monitor for excessive anticholinergic effects, sedation, and somnolence.
Chlophedianol; Dexchlorpheniramine; Pseudoephedrine: (Major) Pseudoephedrine can potentiate the effects and increase the toxicity of other sympathomimetics by adding to their sympathomimetic activity. Although no data are available, pseudoephedrine should be used cautiously in patients using significant quantities of other sympathomimetics.
Chlordiazepoxide: (Moderate) The therapeutic effect of phenylephrine may be decreased in patients receiving benzodiazepines. Monitor patients for decreased pressor effect if these agents are administered concomitantly.
Chlordiazepoxide; Clidinium: (Moderate) The therapeutic effect of phenylephrine may be decreased in patients receiving benzodiazepines. Monitor patients for decreased pressor effect if these agents are administered concomitantly.
Chlorothiazide: (Moderate) The cardiovascular effects of sympathomimetics may reduce the antihypertensive effects produced by diuretics. Well-controlled hypertensive patients receiving decongestant sympathomimetics at recommended doses do not appear at high risk for significant elevations in blood pressure, however, increased blood pressure has been reported in some patients.
Chlorpheniramine; Codeine: (Moderate) Concomitant use of opioid agonists with chlorpheniramine may cause excessive sedation and somnolence. Limit the use of opioid pain medication with chlorpheniramine to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect.
Chlorpheniramine; Dihydrocodeine; Phenylephrine: (Moderate) Concomitant use of opioid agonists with chlorpheniramine may cause excessive sedation and somnolence. Limit the use of opioid pain medication with chlorpheniramine to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect.
Chlorpheniramine; Dihydrocodeine; Pseudoephedrine: (Major) Pseudoephedrine can potentiate the effects and increase the toxicity of other sympathomimetics by adding to their sympathomimetic activity. Although no data are available, pseudoephedrine should be used cautiously in patients using significant quantities of other sympathomimetics. (Moderate) Concomitant use of opioid agonists with chlorpheniramine may cause excessive sedation and somnolence. Limit the use of opioid pain medication

with chlorpheniramine to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect.

Chlorpheniramine; Guaifenesin; Hydrocodone; Pseudoephedrine: (Major) Pseudoephedrine can potentiate the effects and increase the toxicity of other sympathomimetics by adding to their sympathomimetic activity. Although no data are available, pseudoephedrine should be used cautiously in patients using significant quantities of other sympathomimetics. (Moderate) Concomitant use of opioid agonists with chlorpheniramine may cause excessive sedation and somnolence. Limit the use of opioid pain medication with chlorpheniramine to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect.

Chlorpheniramine; Hydrocodone: (Moderate) Concomitant use of opioid agonists with chlorpheniramine may cause excessive sedation and somnolence. Limit the use of opioid pain medication with chlorpheniramine to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect.

Chlorpheniramine; Hydrocodone; Phenylephrine: (Moderate) Concomitant use of opioid agonists with chlorpheniramine may cause excessive sedation and somnolence. Limit the use of opioid pain medication with chlorpheniramine to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect.

Chlorpheniramine; Hydrocodone; Pseudoephedrine: (Major) Pseudoephedrine can potentiate the effects and increase the toxicity of other sympathomimetics by adding to their sympathomimetic activity. Although no data are available, pseudoephedrine should be used cautiously in patients using significant quantities of other sympathomimetics. (Moderate) Concomitant use of opioid agonists with chlorpheniramine may cause excessive sedation and somnolence. Limit the use of opioid pain medication with chlorpheniramine to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect.

Chlorpheniramine; Pseudoephedrine: (Major) Pseudoephedrine can potentiate the effects and increase the toxicity of other sympathomimetics by adding to their sympathomimetic activity. Although no data are available, pseudoephedrine should be used cautiously in patients using significant quantities of other sympathomimetics.

Chlorpromazine: (Moderate) Additive anticholinergic and sedative effects may be seen when chlorpromazine is used with first generation antihistamines, such as chlorpheniramine. Patients should be informed to read non-prescription cough and cold product labels carefully for additional interacting antihistamines.

Chlorthalidone: (Moderate) The cardiovascular effects of sympathomimetics may reduce the antihypertensive effects produced by diuretics. Well-controlled hypertensive patients receiving decongestant sympathomimetics at recommended doses do not appear at high risk for significant elevations in blood pressure, however, increased blood pressure has been reported in some patients.

Chlorthalidone; Clonidine: (Major) The cardiovascular effects of sympathomimetics, such as phenylephrine, may reduce the antihypertensive effects produced by clonidine. Blood pressure and heart rates should be monitored closely to confirm that the desired antihypertensive effect is achieved. (Moderate) The cardiovascular effects of sympathomimetics may reduce the antihypertensive effects produced by diuretics. Well-controlled hypertensive patients receiving decongestant sympathomimetics at

recommended doses do not appear at high risk for significant elevations in blood pressure, however, increased blood pressure has been reported in some patients.
Chlorzoxazone: (Moderate) Additive CNS depression is possible if chlorzoxazone is used concomitantly with other CNS depressants including sedating H1-blockers. Additive effects of sedation and dizziness can occur, which can impair the ability to undertake tasks requiring mental alertness. Dosage adjustments of one or both medications may be necessary.
Ciclesonide: (Moderate) The therapeutic effect of phenylephrine may be increased in patient receiving corticosteroids, such as hydrocortisone. Monitor patients for increased pressor effect if these agents are administered concomitantly.
Clevidipine: (Moderate) Phenylephrine's cardiovascular effects may reduce the antihypertensive effects of calcium-channel blockers. Well-controlled hypertensive patients receiving decongestant sympathomimetics at recommended doses do not appear to be at high risk for significant elevations in blood pressure; however, increased blood pressure (especially systolic hypertension) has been reported in some patients.
Clobazam: (Moderate) Clobazam, a benzodiazepine, may cause drowsiness or other CNS effects. Additive drowsiness may occur when clobazam is combined with CNS depressants such as sedating H1-blockers. In addition, caution is recommended when administering clobazam with medications extensively metabolized by CYP2D6 such as diphenhydramine because clobazam has been shown to inhibit CYP2D6 in vivo and may increase concentrations of drugs metabolized by this enzyme.
Clonazepam: (Moderate) The therapeutic effect of phenylephrine may be decreased in patients receiving benzodiazepines. Monitor patients for decreased pressor effect if these agents are administered concomitantly.
Clonidine: (Major) The cardiovascular effects of sympathomimetics, such as phenylephrine, may reduce the antihypertensive effects produced by clonidine. Blood pressure and heart rates should be monitored closely to confirm that the desired antihypertensive effect is achieved.
Clorazepate: (Moderate) The therapeutic effect of phenylephrine may be decreased in patients receiving benzodiazepines. Monitor patients for decreased pressor effect if these agents are administered concomitantly.
Clozapine: (Moderate) Clozapine exhibits clinically significant anticholinergic effects and sedation that may be additive with other medications that may cause anticholinergic effects and sedation, including antihistamines such as chlorpheniramine. Patients should be informed to read non-prescription cough and cold product labels carefully for additional interacting antihistamines and to avoid tasks requiring mental alertness until they are aware of the effects of the combination.
Cobicistat: (Moderate) Caution is warranted when cobicistat is administered with chlorpheniramine as there is a potential for elevated chlorpheniramine and cobicistat concentrations. Chlorpheniramine is a CYP2D6 substrate/inhibitor. Cobicistat is a substrate/inhibitor of CYP2D6.
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) Concomitant use of opioid agonists with chlorpheniramine may cause excessive sedation and somnolence. Limit the use of opioid pain medication with chlorpheniramine to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect.
Codeine; Guaifenesin: (Moderate) Concomitant use of opioid agonists with chlorpheniramine may cause

excessive sedation and somnolence. Limit the use of opioid pain medication with chlorpheniramine to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect.
Codeine; Phenylephrine; Promethazine: (Moderate) Additive anticholinergic and sedative effects may be seen when promethazine is used with first generation antihistamines, such as chlorpheniramine. Patients should be informed to read non-prescription cough and cold product labels carefully for additional interacting antihistamines. (Moderate) Concomitant use of opioid agonists with chlorpheniramine may cause excessive sedation and somnolence. Limit the use of opioid pain medication with chlorpheniramine to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect.
Codeine; Promethazine: (Moderate) Additive anticholinergic and sedative effects may be seen when promethazine is used with first generation antihistamines, such as chlorpheniramine. Patients should be informed to read non-prescription cough and cold product labels carefully for additional interacting antihistamines. (Moderate) Concomitant use of opioid agonists with chlorpheniramine may cause excessive sedation and somnolence. Limit the use of opioid pain medication with chlorpheniramine to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect.
Colchicine: (Minor) The response to sympathomimetics may be enhanced by colchicine.
Colchicine; Probenecid: (Minor) The response to sympathomimetics may be enhanced by colchicine.
COMT inhibitors: (Moderate) COMT inhibitors should be given cautiously with other agents that cause CNS depression, including sedating H1-blockers, due to the possibility of additive sedation. COMT inhibitors have also been associated with sudden sleep onset during activities of daily living such as driving, which has resulted in accidents in some cases. Prescribers should re-assess patients for drowsiness or sleepiness regularly throughout treatment, especially since events may occur well after the start of treatment. Patients should be advised to avoid driving or other tasks requiring mental alertness until they know how the combination affects them.
Corticosteroids: (Moderate) The therapeutic effect of phenylephrine may be increased in patient receiving corticosteroids, such as hydrocortisone. Monitor patients for increased pressor effect if these agents are administered concomitantly.
Cortisone: (Moderate) The therapeutic effect of phenylephrine may be increased in patient receiving corticosteroids, such as hydrocortisone. Monitor patients for increased pressor effect if these agents are administered concomitantly.
Cyclobenzaprine: (Moderate) Cyclobenzaprine and sedating antihistamines such as chlorpheniramine both exhibit anticholinergic activity, and anticholinergic side effects can be additive. Monitor for anticholinergic-related effects such as constipation and urinary retention. Additive CNS depression causing sedation and/or dizziness is also possible. Dosage adjustments of either or both drugs may be necessary.
Dantrolene: (Moderate) Because sedating H1-blockers cause sedation, an enhanced CNS depressant effect (e.g., drowsiness) may occur when dantrolene is combined with other CNS depressants.
Dapagliflozin: (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.

Dapagliflozin; Metformin: (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.
Dapagliflozin; Saxagliptin: (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.
Daratumumab; Hyaluronidase: (Minor) H1-blockers (antihistamines), when given in large systemic doses, may render tissues partially resistant to the action of hyaluronidase. Patients receiving these medications may require larger amounts of hyaluronidase for equivalent dispersing effect.
Darunavir; Cobicistat: (Moderate) Caution is warranted when cobicistat is administered with chlorpheniramine as there is a potential for elevated chlorpheniramine and cobicistat concentrations. Chlorpheniramine is a CYP2D6 substrate/inhibitor. Cobicistat is a substrate/inhibitor of CYP2D6.
Darunavir; Cobicistat; Emtricitabine; Tenofovir alafenamide: (Moderate) Caution is warranted when cobicistat is administered with chlorpheniramine as there is a potential for elevated chlorpheniramine and cobicistat concentrations. Chlorpheniramine is a CYP2D6 substrate/inhibitor. Cobicistat is a substrate/inhibitor of CYP2D6.
Dasabuvir; Ombitasvir; Paritaprevir; Ritonavir: (Moderate) Concurrent administration of chlorpheniramine with ritonavir may result in elevated plasma concentrations of chlorpheniramine. Chlorpheniramine is metabolized by the hepatic isoenzyme CYP2D6; ritonavir is an inhibitor of this enzyme. Monitor for adverse effects if these drugs are administered together.
Deflazacort: (Moderate) The therapeutic effect of phenylephrine may be increased in patient receiving corticosteroids, such as hydrocortisone. Monitor patients for increased pressor effect if these agents are administered concomitantly.
Desloratadine: (Minor) Although desloratadine is considered a 'non-sedating' antihistamine, dose-related sedation has been noted. For this reason, it would be prudent to monitor for drowsiness during concurrent use of desloratadine with CNS depressants such as other H1-blockers.
Desloratadine; Pseudoephedrine: (Major) Pseudoephedrine can potentiate the effects and increase the toxicity of other sympathomimetics by adding to their sympathomimetic activity. Although no data are available, pseudoephedrine should be used cautiously in patients using significant quantities of other sympathomimetics. (Minor) Although desloratadine is considered a 'non-sedating' antihistamine, dose-related sedation has been noted. For this reason, it would be prudent to monitor for drowsiness during concurrent use of desloratadine with CNS depressants such as other H1-blockers.
Desmopressin: (Moderate) Although the pressor activity of desmopressin is very low compared to its antidiuretic activity, large doses of desmopressin should be used with other pressor agents like phenylephrine only with careful patient monitoring.
Deutetrabenazine: (Moderate) Advise patients that concurrent use of deutetrabenazine and drugs that can

cause CNS depression, such as chlorpheniramine, may have additive effects and worsen drowsiness or sedation.
Dexamethasone: (Moderate) The therapeutic effect of phenylephrine may be increased in patient receiving corticosteroids, such as hydrocortisone. Monitor patients for increased pressor effect if these agents are administered concomitantly.
Dexchlorpheniramine; Dextromethorphan; Pseudoephedrine: (Major) Pseudoephedrine can potentiate the effects and increase the toxicity of other sympathomimetics by adding to their sympathomimetic activity. Although no data are available, pseudoephedrine should be used cautiously in patients using significant quantities of other sympathomimetics.
Dexmedetomidine: (Moderate) Co-administration of dexmedetomidine with sedating antihistamines is likely to lead to an enhancement of CNS depression.
Dexmethylphenidate: (Major) Dexmethylphenidate can potentiate the actions of both exogenous (such as dopamine and epinephrine) and endogenous (such as norepinephrine) vasopressors. It is advisable to monitor cardiac function, including heart rate and blood pressure, if these medications are coadministered. Vasopressors include medications such as epinephrine, dopamine, midodrine, and non-prescription medications including pseudoephedrine and phenylephrine.
Dextroamphetamine: (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; Guaifenesin; Pseudoephedrine: (Major) Pseudoephedrine can potentiate the effects and increase the toxicity of other sympathomimetics by adding to their sympathomimetic activity. Although no data are available, pseudoephedrine should be used cautiously in patients using significant quantities of other sympathomimetics.
Dextromethorphan; Promethazine: (Moderate) Additive anticholinergic and sedative effects may be seen when promethazine is used with first generation antihistamines, such as chlorpheniramine. Patients should be informed to read non-prescription cough and cold product labels carefully for additional interacting antihistamines.
Diazepam: (Moderate) The therapeutic effect of phenylephrine may be decreased in patients receiving benzodiazepines. Monitor patients for decreased pressor effect if these agents are administered concomitantly.
Diethylpropion: (Major) Diethylpropion has vasopressor effects. Coadministration with other vasopressors may have the potential for serious cardiac adverse effects such as hypertensive crisis and cardiac arrhythmias.
Digitoxin: (Major) Concomitant use of cardiac glycosides with sympathomimetics can cause arrhythmias because sympathomimetics enhance ectopic pacemaker activity. Caution is warranted during co-administration of digoxin and sympathomimetics.
Digoxin: (Major) Concomitant use of cardiac glycosides with sympathomimetics can cause arrhythmias because sympathomimetics enhance ectopic pacemaker activity. Caution is warranted during co-administration of digoxin and sympathomimetics.
Dihydrocodeine; Guaifenesin; Pseudoephedrine: (Major) Pseudoephedrine can potentiate the effects and increase the toxicity of other sympathomimetics by adding to their sympathomimetic activity. Although no data are available, pseudoephedrine should be used cautiously in patients using significant quantities of other sympathomimetics. (Moderate) Concomitant use of opioid agonists with chlorpheniramine may cause excessive sedation and somnolence. Limit the use of opioid pain medication

with chlorpheniramine to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect.

Dihydroergotamine: (Severe) Ergot alkaloids should not be administered with vasoconstrictors such as vasopressors (e.g., norepinephrine, dopamine, phenylephrine) since combining these agents may produce a synergistic increase in blood pressure. There is also an additive risk of peripheral ischemia or gangrene. Of note, at therapeutic doses, ergoloid mesylates lack the vasoconstrictor properties of the natural ergot alkaloids; therefore, ergoloid mesylates are not expected to interact with sympathomimetics.

Diltiazem: (Moderate) Phenylephrine's cardiovascular effects may reduce the antihypertensive effects of calcium-channel blockers. Well-controlled hypertensive patients receiving decongestant sympathomimetics at recommended doses do not appear to be at high risk for significant elevations in blood pressure; however, increased blood pressure (especially systolic hypertension) has been reported in some patients.

Dipeptidyl Peptidase-4 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.

Diphenhydramine; Hydrocodone; Phenylephrine: (Moderate) Concomitant use of opioid agonists with chlorpheniramine may cause excessive sedation and somnolence. Limit the use of opioid pain medication with chlorpheniramine to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect.

Disopyramide: (Moderate) The anticholinergic effects of sedating H1-blockers may be enhanced when combined with other drugs with moderate to significant anticholinergic effects including disopyramide. Clinicians should note that antimuscarinic effects might be seen not only on GI smooth muscle, but also on bladder function, the eye, and temperature regulation.

Donepezil: (Moderate) Concurrent use of sedating H1-blockers and donepezil should be avoided if possible. Donepezil inhibits acetylcholinesterase, the enzyme responsible for the degradation of acetylcholine, and improves the availability of acetylcholine. Sedating H1-blockers may exhibit significant anticholinergic activity, thereby interfering with the therapeutic effect of donepezil.

Donepezil; Memantine: (Moderate) Concurrent use of sedating H1-blockers and donepezil should be avoided if possible. Donepezil inhibits acetylcholinesterase, the enzyme responsible for the degradation of acetylcholine, and improves the availability of acetylcholine. Sedating H1-blockers may exhibit significant anticholinergic activity, thereby interfering with the therapeutic effect of donepezil.

Dorzolamide; Timolol: (Minor) Close monitoring of blood pressure or the selection of alternative therapeutic agents to the sympathomimetic agent may be needed in patients receiving a beta-blocker. Sympathomimetics, such as amphetamines, phentermine, and decongestants (e.g., pseudoephedrine, phenylephrine), and many other drugs, may increase both systolic and diastolic blood pressure and may counteract the activity of the beta-blockers. Concurrent use increases the risk of unopposed alpha-adrenergic activity. Increased blood pressure, bradycardia, or heart block may occur due to excessive alpha-adrenergic receptor stimulation.

Doxazosin: (Major) Sympathomimetics can antagonize the effects of antihypertensives such as alpha-

blockers when administered concomitantly.
Doxorubicin: (Major) Chlorpheniramine is a CYP2D6 inhibitor and doxorubicin is a major CYP2D6 substrate. Clinically significant interactions have been reported when doxorubicin was coadministered with inhibitors of CYP2D6, resulting in increased concentration and clinical effect of doxorubicin. Avoid coadministration of chlorpheniramine and doxorubicin if possible. If not possible, closely monitor for increased side effects of doxorubicin including myelosuppression and cardiotoxicity.
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. (Moderate) Use caution if coadministration of dronabinol with antihistamines is necessary. Concurrent use of dronabinol, THC with antihistamines may result in additive drowsiness, hypertension, tachycardia, and possibly cardiotoxicity.
Dronedarone: (Moderate) Dronedarone is an inhibitor of CYP2D6. Chlorpheniramine is a substrate for CYP2D6. The concomitant administration of dronedarone and CYP2D6 substrates may result in increased exposure of the substrate and should, therefore, be undertaken with caution.
Droperidol: (Moderate) Sedating H1-blockers have additive or potentiating sedative and other CNS effects with droperidol. Following administration of droperidol, lower doses of the other CNS depressant may need to be used.
Dulaglutide: (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.
Dutasteride; Tamsulosin: (Moderate) Use caution when administering tamsulosin with a moderate CYP2D6 inhibitor such as chlorpheniramine. Tamsulosin is extensively metabolized by CYP2D6 hepatic enzymes. In clinical evaluation, concomitant treatment with a strong CYP2D6 inhibitor resulted in increases in tamsulosin exposure; interactions with moderate CYP2D6 inhibitors have not been evaluated. If concomitant use in necessary, monitor patient closely for increased side effects.
Dyphylline: (Moderate) Use of sympathomimetics with dyphylline should be approached with caution. Coadministration may lead to adverse effects, such as tremors, insomnia, seizures, or cardiac arrhythmias.
Dyphylline; Guaifenesin: (Moderate) Use of sympathomimetics with dyphylline should be approached with caution. Coadministration may lead to adverse effects, such as tremors, insomnia, seizures, or cardiac arrhythmias.
Eliglustat: (Major) In extensive or intermediate CYP2D6 metabolizers (EMs or IMs), coadministration of scheduled chlorpheniramine and eliglustat requires dosage reduction of eliglustat to 84 mg PO once daily during the course of antihistamine treatment; however, coadministration of eliglustat with both chlorpheniramine and a strong or moderate CYP3A inhibitor is contraindicated. It is unclear whether a single dose of chlorpheniramine warrants modification of eliglustat therapy. Chlorpheniramine is a substrate and moderate inhibitor of CYP2D6; eliglustat is also a substrate and inhibitor of CYP2D6 as well as a CYP3A substrate. Coadministration of eliglustat with CYP2D6 inhibitors, such as chlorpheniramine, may increase eliglustat exposure and the risk of serious adverse events (e.g., QT prolongation and cardiac

arrhythmias); the effects of a single chlorpheniramine dose are unknown. In addition, coadministration of eliglustat with CYP2D6 substrates (e.g., chlorpheniramine) may result in increased concentrations of the concomitant drug; monitor patients closely for anticholinergic adverse events.

Elvitegravir; Cobicistat; Emtricitabine; Tenofovir Alafenamide: (Moderate) Caution is warranted when cobicistat is administered with chlorpheniramine as there is a potential for elevated chlorpheniramine and cobicistat concentrations. Chlorpheniramine is a CYP2D6 substrate/inhibitor. Cobicistat is a substrate/inhibitor of CYP2D6.

Elvitegravir; Cobicistat; Emtricitabine; Tenofovir Disoproxil Fumarate: (Moderate) Caution is warranted when cobicistat is administered with chlorpheniramine as there is a potential for elevated chlorpheniramine and cobicistat concentrations. Chlorpheniramine is a CYP2D6 substrate/inhibitor. Cobicistat is a substrate/inhibitor of CYP2D6.

Empagliflozin: (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.

Empagliflozin; Linagliptin: (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.

Empagliflozin; Linagliptin; Metformin: (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.

Empagliflozin; Metformin: (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.

Enalapril; Felodipine: (Moderate) Phenylephrine's cardiovascular effects may reduce the antihypertensive effects of calcium-channel blockers. Well-controlled hypertensive patients receiving decongestant sympathomimetics at recommended doses do not appear to be at high risk for significant

elevations in blood pressure; however, increased blood pressure (especially systolic hypertension) has been reported in some patients.
Enalapril; Hydrochlorothiazide, HCTZ: (Moderate) The cardiovascular effects of sympathomimetics may reduce the antihypertensive effects produced by diuretics. Well-controlled hypertensive patients receiving decongestant sympathomimetics at recommended doses do not appear at high risk for significant elevations in blood pressure, however, increased blood pressure has been reported in some patients.
Enflurane: (Major) Halogenated anesthetics may sensitize the myocardium to the effects of sympathomimetics, including phenylephrine, which can increase the risk of developing cardiac arrhythmias and hypotension.
Entacapone: (Moderate) COMT inhibitors should be given cautiously with other agents that cause CNS depression, including sedating H1-blockers, due to the possibility of additive sedation. COMT inhibitors have also been associated with sudden sleep onset during activities of daily living such as driving, which has resulted in accidents in some cases. Prescribers should re-assess patients for drowsiness or sleepiness regularly throughout treatment, especially since events may occur well after the start of treatment. Patients should be advised to avoid driving or other tasks requiring mental alertness until they know how the combination affects them.
Epinephrine: (Major) Because epinephrine is a sympathomimetic drug with agonist actions at both the alpha and beta receptors, caution is warranted in patients receiving epinephrine concomitantly with other sympathomimetics as additive pharmacodynamic effects are possible, some which may be undesirable.
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.
Eprosartan; Hydrochlorothiazide, HCTZ: (Moderate) The cardiovascular effects of sympathomimetics may reduce the antihypertensive effects produced by diuretics. Well-controlled hypertensive patients receiving decongestant sympathomimetics at recommended doses do not appear at high risk for significant elevations in blood pressure, however, increased blood pressure has been reported in some patients.
Ergoloid Mesylates: (Severe) Ergot alkaloids should not be administered with vasoconstrictors such as vasopressors (e.g., norepinephrine, dopamine, phenylephrine) since combining these agents may produce a synergistic increase in blood pressure. There is also an additive risk of peripheral ischemia or gangrene. Of note, at therapeutic doses, ergoloid mesylates lack the vasoconstrictor properties of the natural ergot alkaloids; therefore, ergoloid mesylates are not expected to interact with sympathomimetics.
Ergonovine: (Severe) Ergot alkaloids should not be administered with vasoconstrictors such as vasopressors (e.g., norepinephrine, dopamine, phenylephrine) since combining these agents may produce a synergistic increase in blood pressure. There is also an additive risk of peripheral ischemia or gangrene. Of note, at therapeutic doses, ergoloid mesylates lack the vasoconstrictor properties of the natural ergot alkaloids; therefore, ergoloid mesylates are not expected to interact with sympathomimetics.
Ergot alkaloids: (Severe) Ergot alkaloids should not be administered with vasoconstrictors such as vasopressors (e.g., norepinephrine, dopamine, phenylephrine) since combining these agents may produce a synergistic increase in blood pressure. There is also an additive risk of peripheral ischemia or gangrene. Of note, at therapeutic doses, ergoloid mesylates lack the vasoconstrictor properties of the natural ergot alkaloids; therefore, ergoloid mesylates are not expected to interact with sympathomimetics.

Ergotamine: (Severe) Ergot alkaloids should not be administered with vasoconstrictors such as vasopressors (e.g., norepinephrine, dopamine, phenylephrine) since combining these agents may produce a synergistic increase in blood pressure. There is also an additive risk of peripheral ischemia or gangrene. Of note, at therapeutic doses, ergoloid mesylates lack the vasoconstrictor properties of the natural ergot alkaloids; therefore, ergoloid mesylates are not expected to interact with sympathomimetics.
Ertugliflozin: (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.
Ertugliflozin; Metformin: (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.
Ertugliflozin; Sitagliptin: (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.
Esketamine: (Moderate) Closely monitor patients receiving esketamine and chlorpheniramine for sedation and other CNS depressant effects. Instruct patients who receive a dose of esketamine not to drive or engage in other activities requiring alertness until the next day after a restful sleep.
Esmolol: (Minor) Close monitoring of blood pressure or the selection of alternative therapeutic agents to the sympathomimetic agent may be needed in patients receiving a beta-blocker. Sympathomimetics, such as amphetamines, phentermine, and decongestants (e.g., pseudoephedrine, phenylephrine), and many other drugs, may increase both systolic and diastolic blood pressure and may counteract the activity of the beta-blockers. Concurrent use increases the risk of unopposed alpha-adrenergic activity. Increased blood pressure, bradycardia, or heart block may occur due to excessive alpha-adrenergic receptor stimulation.
Estazolam: (Moderate) The therapeutic effect of phenylephrine may be decreased in patients receiving benzodiazepines. Monitor patients for decreased pressor effect if these agents are administered concomitantly.
Eszopiclone: (Moderate) A reduction in the dose of eszopiclone and concomitantly administered CNS depressants, such as sedating H1-blockers, should be considered to minimize additive sedative effects. In addition, the risk of next-day psychomotor impairment is increased during co-administration of eszopiclone and other CNS depressants, which may decrease the ability to perform tasks requiring full mental alertness such as driving.

Ethacrynic Acid: (Moderate) The cardiovascular effects of sympathomimetics may reduce the antihypertensive effects produced by diuretics. Well-controlled hypertensive patients receiving decongestant sympathomimetics at recommended doses do not appear at high risk for significant elevations in blood pressure, however, increased blood pressure has been reported in some patients.
Ethanol: (Moderate) Drowsiness may occur with the use of sedating antihistamines. Caution patients about the simultaneous use of alcohol, and caution that the effects of alcohol may be increased. Additive drowsiness and psychomotor impairment may occur.
Etomidate: (Minor) Because sedating H1-blockers cause sedation, an enhanced CNS depressant effect may occur when they are combined with general anesthetics.
Everolimus: (Moderate) Monitor for an increase in chlorpheniramine-related adverse reactions if coadministration with everolimus is necessary. Chlorpheniramine is a CYP2D6 substrate and everolimus is a CYP2D6 inhibitor.
Exenatide: (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.
Ezogabine: (Moderate) Caution is advisable during concurrent use of ezogabine and medications that may affect voiding such as chlorpheniramine, a sedating antihistamine (H1-blocker). Ezogabine has caused urinary retention requiring catheterization in some cases. The anticholinergic effects of chlorpheniramine on the urinary tract may be additive. Additive sedation or other CNS effects may also occur.
Felodipine: (Moderate) Phenylephrine's cardiovascular effects may reduce the antihypertensive effects of calcium-channel blockers. Well-controlled hypertensive patients receiving decongestant sympathomimetics at recommended doses do not appear to be at high risk for significant elevations in blood pressure; however, increased blood pressure (especially systolic hypertension) has been reported in some patients.
Fenfluramine: (Moderate) Monitor for excessive sedation and somnolence during coadministration of fenfluramine and chlorpheniramine. Concurrent use may result in additive CNS depression.
Fentanyl: (Major) Pain control may be impaired if fentanyl nasal spray is administered in patients receiving vasoconstrictive nasal decongestants (e.g., phenylephrine); do not titrate fentanyl nasal spray dose in such patients. This interaction is not expected with other fentanyl administration routes. (Moderate) Concomitant use of opioid agonists with chlorpheniramine may cause excessive sedation and somnolence. Limit the use of opioid pain medication with chlorpheniramine to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect.
Fexofenadine; Pseudoephedrine: (Major) Pseudoephedrine can potentiate the effects and increase the toxicity of other sympathomimetics by adding to their sympathomimetic activity. Although no data are available, pseudoephedrine should be used cautiously in patients using significant quantities of other sympathomimetics.
Flibanserin: (Moderate) The concomitant use of flibanserin with CNS depressants, such as sedating H1-blockers, may increase the risk of CNS depression (e.g., dizziness, somnolence) compared to the use of flibanserin alone. Patients should avoid activities requiring full alertness (e.g., operating machinery or driving) until at least 6 hours after each dose and until they know how flibanserin affects them.

Fludrocortisone: (Moderate) The therapeutic effect of phenylephrine may be increased in patient receiving corticosteroids, such as hydrocortisone. Monitor patients for increased pressor effect if these agents are administered concomitantly.
Flunisolide: (Moderate) The therapeutic effect of phenylephrine may be increased in patient receiving corticosteroids, such as hydrocortisone. Monitor patients for increased pressor effect if these agents are administered concomitantly.
Fluoxetine; Olanzapine: (Moderate) Olanzapine exhibits anticholinergic effects that may be clinically significant. Clinicians should keep this in mind when using antimuscarinics and other medications with anticholinergic activity in combination with olanzapine. Some medications exhibit additive anticholinergic effects include sedating H1-blockers. Olanzapine may also cause additive sedation with many of these drugs.
Fluphenazine: (Moderate) Additive sedative effects may be seen when fluphenazine is used with first generation antihistamines, such as chlorpheniramine. Patients should be informed to read non-prescription cough and cold product labels carefully for additional interacting antihistamines.
Flurazepam: (Moderate) The therapeutic effect of phenylephrine may be decreased in patients receiving benzodiazepines. Monitor patients for decreased pressor effect if these agents are administered concomitantly.
Fluticasone: (Moderate) The therapeutic effect of phenylephrine may be increased in patient receiving corticosteroids, such as hydrocortisone. Monitor patients for increased pressor effect if these agents are administered concomitantly.
Fluticasone; Salmeterol: (Moderate) Caution and close observation should also be used when salmeterol is used concurrently with other adrenergic sympathomimetics, administered by any route, to avoid potential for increased cardiovascular effects. (Moderate) The therapeutic effect of phenylephrine may be increased in patient receiving corticosteroids, such as hydrocortisone. Monitor patients for increased pressor effect if these agents are administered concomitantly.
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. (Moderate) The therapeutic effect of phenylephrine may be increased in patient receiving corticosteroids, such as hydrocortisone. Monitor patients for increased pressor effect if these agents are administered concomitantly.
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. (Moderate) The therapeutic effect of phenylephrine may be increased in patient receiving corticosteroids, such as hydrocortisone. Monitor patients for increased pressor effect if these agents are administered concomitantly.
Formoterol: (Moderate) Caution and close observation should be used when formoterol is used concurrently with other adrenergic sympathomimetics, administered by any route, to avoid potential for increased cardiovascular effects.
Formoterol; Mometasone: (Moderate) Caution and close observation should be used when formoterol is used concurrently with other adrenergic sympathomimetics, administered by any route, to avoid potential for increased cardiovascular effects. (Moderate) The therapeutic effect of phenylephrine may be increased in patient receiving corticosteroids, such as hydrocortisone. Monitor patients for increased pressor effect if these agents are administered concomitantly.
Fosinopril; Hydrochlorothiazide, HCTZ: (Moderate) The cardiovascular effects of sympathomimetics

may reduce the antihypertensive effects produced by diuretics. Well-controlled hypertensive patients receiving decongestant sympathomimetics at recommended doses do not appear at high risk for significant elevations in blood pressure, however, increased blood pressure has been reported in some patients.
Fospropofol: (Minor) Because sedating H1-blockers cause sedation, an enhanced CNS depressant effect may occur when they are combined with general anesthetics like fospropofol.
Furosemide: (Moderate) The cardiovascular effects of sympathomimetics may reduce the antihypertensive effects produced by diuretics. Well-controlled hypertensive patients receiving decongestant sympathomimetics at recommended doses do not appear at high risk for significant elevations in blood pressure, however, increased blood pressure has been reported in some patients.
Gabapentin: (Moderate) Monitor for excessive sedation and somnolence during coadministration of chlorpheniramine and gabapentin. Concurrent use may result in additive CNS depression.
Galantamine: (Moderate) Concurrent use of sedating H1-blockers and galantamine should be avoided if possible. Galantamine inhibits acetylcholinesterase, the enzyme responsible for the degradation of acetylcholine, and improves the availability of acetylcholine. Sedating H1-blockers may exhibit significant anticholinergic activity, thereby interfering with the therapeutic effect of galantamine.
Gentamicin: (Minor) Chlorpheniramine may effectively mask vestibular symptoms (e.g. dizziness, tinnitus, or vertigo) that are associated with ototoxicity induced by aminoglycosides. Antiemetics block the histamine or acetylcholine response that causes nausea due to vestibular emetic stimuli such as motion.
Ginger, Zingiber officinale: (Minor) In vitro studies have demonstrated the positive inotropic effects of certain gingerol constituents of ginger; but it is unclear if whole ginger root exhibits these effects clinically in humans. It is theoretically possible that excessive doses of ginger could affect the action of vasopressors like phenylephrine; however, no clinical data are available.
Glimepiride; Pioglitazone: (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.
Glimepiride; Rosiglitazone: (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.
Glipizide; Metformin: (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.

Glyburide; Metformin: (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.
Glycopyrrolate; Formoterol: (Moderate) Caution and close observation should be used when formoterol is used concurrently with other adrenergic sympathomimetics, administered by any route, to avoid potential for increased cardiovascular effects.
Green Tea: (Moderate) Some, but not all, green tea products contain caffeine. Caffeine should be avoided or used cautiously with phenylephrine. CNS stimulants and sympathomimetics are associated with adverse effects such as nervousness, irritability, insomnia, and cardiac arrhythmias.
Guaifenesin; Hydrocodone: (Moderate) Concomitant use of opioid agonists with chlorpheniramine may cause excessive sedation and somnolence. Limit the use of opioid pain medication with chlorpheniramine to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect.
Guaifenesin; Hydrocodone; Pseudoephedrine: (Major) Pseudoephedrine can potentiate the effects and increase the toxicity of other sympathomimetics by adding to their sympathomimetic activity. Although no data are available, pseudoephedrine should be used cautiously in patients using significant quantities of other sympathomimetics. (Moderate) Concomitant use of opioid agonists with chlorpheniramine may cause excessive sedation and somnolence. Limit the use of opioid pain medication with chlorpheniramine to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect.
Guaifenesin; Pseudoephedrine: (Major) Pseudoephedrine can potentiate the effects and increase the toxicity of other sympathomimetics by adding to their sympathomimetic activity. Although no data are available, pseudoephedrine should be used cautiously in patients using significant quantities of other sympathomimetics.
Guanabenz: (Moderate) Sympathomimetics can antagonize the antihypertensive effects of guanabenz when administered concomitantly. Patients should be monitored for loss of blood pressure control.
Halogenated Anesthetics: (Minor) Because sedating H1-blockers cause sedation, an enhanced CNS depressant effect may occur when they are combined with general anesthetics.
Haloperidol: (Moderate) Haloperidol can potentiate the actions of other CNS depressants such as the sedating H1-blockers. Additive anticholinergic effects may occur. Clinicians should note that antimuscarinic effects may be seen not only on GI smooth muscle, but also on bladder function, the eye, and temperature regulation. Additive drowsiness or CNS effects may also occur. (Moderate) Non-cardiovascular drugs with alpha-blocking activity such as haloperidol, directly counteract the effects of phenylephrine and can counter the desired pharmacologic effect. They also can be used to treat excessive phenylephrine-induced hypertension.
Halothane: (Major) Halogenated anesthetics may sensitize the myocardium to the effects of sympathomimetics, including phenylephrine, which can increase the risk of developing cardiac arrhythmias and hypotension.
Heparin: (Minor) Antihistamines may partially counteract the anticoagulant actions of heparin, according to the product labels. However, this interaction is not likely of clinical significance since heparin therapy is adjusted to the partial thromboplastin time (aPTT) and other clinical parameters of the patient.

Homatropine; Hydrocodone: (Moderate) Concomitant use of opioid agonists with chlorpheniramine may cause excessive sedation and somnolence. Limit the use of opioid pain medication with chlorpheniramine to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect.
Hyaluronidase, Recombinant; Immune Globulin: (Minor) H1-blockers (antihistamines), when given in large systemic doses, may render tissues partially resistant to the action of hyaluronidase. Patients receiving these medications may require larger amounts of hyaluronidase for equivalent dispersing effect.
Hyaluronidase: (Minor) H1-blockers (antihistamines), when given in large systemic doses, may render tissues partially resistant to the action of hyaluronidase. Patients receiving these medications may require larger amounts of hyaluronidase for equivalent dispersing effect.
Hydantoins: (Moderate) Hydantoin anticonvulsants can theoretically add to the CNS depressant effects of other CNS depressants including the sedating H1 blockers.
Hydralazine; Hydrochlorothiazide, HCTZ: (Moderate) The cardiovascular effects of sympathomimetics may reduce the antihypertensive effects produced by diuretics. Well-controlled hypertensive patients receiving decongestant sympathomimetics at recommended doses do not appear at high risk for significant elevations in blood pressure, however, increased blood pressure has been reported in some patients.
Hydrochlorothiazide, HCTZ: (Moderate) The cardiovascular effects of sympathomimetics may reduce the antihypertensive effects produced by diuretics. Well-controlled hypertensive patients receiving decongestant sympathomimetics at recommended doses do not appear at high risk for significant elevations in blood pressure, however, increased blood pressure has been reported in some patients.
Hydrochlorothiazide, HCTZ; Irbesartan: (Moderate) The cardiovascular effects of sympathomimetics may reduce the antihypertensive effects produced by diuretics. Well-controlled hypertensive patients receiving decongestant sympathomimetics at recommended doses do not appear at high risk for significant elevations in blood pressure, however, increased blood pressure has been reported in some patients.
Hydrochlorothiazide, HCTZ; Lisinopril: (Moderate) The cardiovascular effects of sympathomimetics may reduce the antihypertensive effects produced by diuretics. Well-controlled hypertensive patients receiving decongestant sympathomimetics at recommended doses do not appear at high risk for significant elevations in blood pressure, however, increased blood pressure has been reported in some patients.
Hydrochlorothiazide, HCTZ; Losartan: (Moderate) The cardiovascular effects of sympathomimetics may reduce the antihypertensive effects produced by diuretics. Well-controlled hypertensive patients receiving decongestant sympathomimetics at recommended doses do not appear at high risk for significant elevations in blood pressure, however, increased blood pressure has been reported in some patients.
Hydrochlorothiazide, HCTZ; Methyldopa: (Major) Sympathomimetics, such as phenylephrine, can antagonize the antihypertensive effects of methyldopa when administered concomitantly. Blood pressure should be monitored closely to confirm that the desired antihypertensive effect is achieved. (Moderate) The cardiovascular effects of sympathomimetics may reduce the antihypertensive effects produced by diuretics. Well-controlled hypertensive patients receiving decongestant sympathomimetics at recommended doses do not appear at high risk for significant elevations in blood pressure, however, increased blood pressure has been reported in some patients.
Hydrochlorothiazide, HCTZ; Metoprolol: (Moderate) The cardiovascular effects of sympathomimetics may reduce the antihypertensive effects produced by diuretics. Well-controlled hypertensive patients receiving decongestant sympathomimetics at recommended doses do not appear at high risk for significant elevations in blood pressure, however, increased blood pressure has been reported in some patients. (Minor) Close monitoring of blood pressure or the selection of alternative therapeutic agents to the sympathomimetic agent may be needed in patients receiving a beta-blocker. Sympathomimetics, such as amphetamines, phentermine, and decongestants (e.g., pseudoephedrine, phenylephrine), and many other

drugs, may increase both systolic and diastolic blood pressure and may counteract the activity of the beta-blockers. Concurrent use increases the risk of unopposed alpha-adrenergic activity. Increased blood pressure, bradycardia, or heart block may occur due to excessive alpha-adrenergic receptor stimulation.
Hydrochlorothiazide, HCTZ; Moexipril: (Moderate) The cardiovascular effects of sympathomimetics may reduce the antihypertensive effects produced by diuretics. Well-controlled hypertensive patients receiving decongestant sympathomimetics at recommended doses do not appear at high risk for significant elevations in blood pressure, however, increased blood pressure has been reported in some patients.
Hydrochlorothiazide, HCTZ; Olmesartan: (Moderate) The cardiovascular effects of sympathomimetics may reduce the antihypertensive effects produced by diuretics. Well-controlled hypertensive patients receiving decongestant sympathomimetics at recommended doses do not appear at high risk for significant elevations in blood pressure, however, increased blood pressure has been reported in some patients.
Hydrochlorothiazide, HCTZ; Propranolol: (Moderate) The cardiovascular effects of sympathomimetics may reduce the antihypertensive effects produced by diuretics. Well-controlled hypertensive patients receiving decongestant sympathomimetics at recommended doses do not appear at high risk for significant elevations in blood pressure, however, increased blood pressure has been reported in some patients. (Minor) Close monitoring of blood pressure or the selection of alternative therapeutic agents to the sympathomimetic agent may be needed in patients receiving a beta-blocker. Sympathomimetics, such as amphetamines, phentermine, and decongestants (e.g., pseudoephedrine, phenylephrine), and many other drugs, may increase both systolic and diastolic blood pressure and may counteract the activity of the beta-blockers. Concurrent use increases the risk of unopposed alpha-adrenergic activity. Increased blood pressure, bradycardia, or heart block may occur due to excessive alpha-adrenergic receptor stimulation.
Hydrochlorothiazide, HCTZ; Quinapril: (Moderate) The cardiovascular effects of sympathomimetics may reduce the antihypertensive effects produced by diuretics. Well-controlled hypertensive patients receiving decongestant sympathomimetics at recommended doses do not appear at high risk for significant elevations in blood pressure, however, increased blood pressure has been reported in some patients.
Hydrochlorothiazide, HCTZ; Spironolactone: (Moderate) The cardiovascular effects of sympathomimetics may reduce the antihypertensive effects produced by diuretics. Well-controlled hypertensive patients receiving decongestant sympathomimetics at recommended doses do not appear at high risk for significant elevations in blood pressure, however, increased blood pressure has been reported in some patients.
Hydrochlorothiazide, HCTZ; Telmisartan: (Moderate) The cardiovascular effects of sympathomimetics may reduce the antihypertensive effects produced by diuretics. Well-controlled hypertensive patients receiving decongestant sympathomimetics at recommended doses do not appear at high risk for significant elevations in blood pressure, however, increased blood pressure has been reported in some patients.
Hydrochlorothiazide, HCTZ; Triamterene: (Moderate) The cardiovascular effects of sympathomimetics may reduce the antihypertensive effects produced by diuretics. Well-controlled hypertensive patients receiving decongestant sympathomimetics at recommended doses do not appear at high risk for significant elevations in blood pressure, however, increased blood pressure has been reported in some patients.
Hydrochlorothiazide, HCTZ; Valsartan: (Moderate) The cardiovascular effects of sympathomimetics may reduce the antihypertensive effects produced by diuretics. Well-controlled hypertensive patients receiving decongestant sympathomimetics at recommended doses do not appear at high risk for significant elevations in blood pressure, however, increased blood pressure has been reported in some patients.
Hydrocodone: (Moderate) Concomitant use of opioid agonists with chlorpheniramine may cause excessive sedation and somnolence. Limit the use of opioid pain medication with chlorpheniramine to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect.

Hydrocodone; Ibuprofen: (Moderate) Concomitant use of opioid agonists with chlorpheniramine may cause excessive sedation and somnolence. Limit the use of opioid pain medication with chlorpheniramine to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect.
Hydrocodone; Phenylephrine: (Moderate) Concomitant use of opioid agonists with chlorpheniramine may cause excessive sedation and somnolence. Limit the use of opioid pain medication with chlorpheniramine to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect.
Hydrocodone; Potassium Guaiacolsulfonate: (Moderate) Concomitant use of opioid agonists with chlorpheniramine may cause excessive sedation and somnolence. Limit the use of opioid pain medication with chlorpheniramine to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect.
Hydrocodone; Potassium Guaiacolsulfonate; Pseudoephedrine: (Major) Pseudoephedrine can potentiate the effects and increase the toxicity of other sympathomimetics by adding to their sympathomimetic activity. Although no data are available, pseudoephedrine should be used cautiously in patients using significant quantities of other sympathomimetics. (Moderate) Concomitant use of opioid agonists with chlorpheniramine may cause excessive sedation and somnolence. Limit the use of opioid pain medication with chlorpheniramine to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect.
Hydrocodone; Pseudoephedrine: (Major) Pseudoephedrine can potentiate the effects and increase the toxicity of other sympathomimetics by adding to their sympathomimetic activity. Although no data are available, pseudoephedrine should be used cautiously in patients using significant quantities of other sympathomimetics. (Moderate) Concomitant use of opioid agonists with chlorpheniramine may cause excessive sedation and somnolence. Limit the use of opioid pain medication with chlorpheniramine to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect.
Hydrocortisone: (Moderate) The therapeutic effect of phenylephrine may be increased in patient receiving corticosteroids, such as hydrocortisone. Monitor patients for increased pressor effect if these agents are administered concomitantly.
Hydromorphone: (Moderate) Concomitant use of opioid agonists with chlorpheniramine may cause excessive sedation and somnolence. Limit the use of opioid pain medication with chlorpheniramine to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect.
Ibuprofen; Oxycodone: (Moderate) Concomitant use of opioid agonists with chlorpheniramine may cause excessive sedation and somnolence. Limit the use of opioid pain medication with chlorpheniramine to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect.
Ibuprofen; Pseudoephedrine: (Major) Pseudoephedrine can potentiate the effects and increase the toxicity of other sympathomimetics by adding to their sympathomimetic activity. Although no data are available, pseudoephedrine should be used cautiously in patients using significant quantities of other sympathomimetics.
Iloperidone: (Moderate) Drugs that can cause CNS depression, if used concomitantly with iloperidone, may increase both the frequency and the intensity of adverse effects such as drowsiness, sedation, and

dizziness. Caution should be used when iloperidone is given in combination with other centrally-acting medications, such as sedating H1-blockers.
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.
Incretin Mimetics: (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.
Indacaterol: (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.
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) Sympathomimetics can antagonize the antihypertensive effects of vasodilators when administered concomitantly. Patients should be monitored to confirm that the desired antihypertensive effect is achieved.
Insulin Degludec; Liraglutide: (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.
Insulin Glargine; Lixisenatide: (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.
Insulins: (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.

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.

Ionic Contrast Media: (Severe) The intravascular injection of a contrast medium should never be made following the administration of vasopressors since they strongly potentiate neurologic effects. Serious neurologic sequelae, including permanent paralysis, have been reported following cerebral arteriography, selective spinal arteriography and arteriography of vessels supplying the spinal cord.

Isocarboxazid: (Severe) 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. (Major) Concurrent use of monoamine oxidase inhibitors (MAOIs) and sedating H1-blockers (antihistamines) may result in additive sedation, anticholinergic effects, or hypotensive reactions. Consider alternative therapy to these antihistamines where possible. If alternative combinations are not available, these medications may be used together with close monitoring. Many nonprescription products for coughs, colds, allergy, hay fever, or insomnia contain sedating antihistamines. Patients receiving an MAOI should be counseled that it is essential to consult their health care provider or pharmacist prior to the use of any nonprescription products. Advise against driving or engaging in other activities requiring mental alertness until patients know how this combination affects them.

Isoflurane: (Major) Halogenated anesthetics may sensitize the myocardium to the effects of sympathomimetics, including phenylephrine, which can increase the risk of developing cardiac arrhythmias and hypotension.

Isradipine: (Moderate) Phenylephrine's cardiovascular effects may reduce the antihypertensive effects of calcium-channel blockers. Well-controlled hypertensive patients receiving decongestant sympathomimetics at recommended doses do not appear to be at high risk for significant elevations in blood pressure; however, increased blood pressure (especially systolic hypertension) has been reported in some patients.

Kanamycin: (Minor) Chlorpheniramine may effectively mask vestibular symptoms (e.g. dizziness, tinnitus, or vertigo) that are associated with ototoxicity induced by aminoglycosides. Antiemetics block the histamine or acetylcholine response that causes nausea due to vestibular emetic stimuli such as motion.

Ketamine: (Minor) Because sedating H1-blockers cause sedation, an enhanced CNS depressant effect may occur when they are combined with general anesthetics.

Labetalol: (Minor) Close monitoring of blood pressure or the selection of alternative therapeutic agents to the sympathomimetic agent may be needed in patients receiving a beta-blocker. Sympathomimetics, such as amphetamines, phentermine, and decongestants (e.g., pseudoephedrine, phenylephrine), and many other drugs, may increase both systolic and diastolic blood pressure and may counteract the activity of the beta-blockers. Concurrent use increases the risk of unopposed alpha-adrenergic activity. Increased blood

pressure, bradycardia, or heart block may occur due to excessive alpha-adrenergic receptor stimulation.
Lasmiditan: (Moderate) Monitor for excessive sedation and somnolence during coadministration of lasmiditan and sedating H1-blockers. Concurrent use may result in additive CNS depression.
Lemborexant: (Moderate) Monitor for excessive sedation and somnolence during coadministration of lemborexant and sedating antihistamines (H1-blockers). Dosage adjustments of lemborexant and sedating H1-blockers may be necessary when administered together because of potentially additive CNS effects. The risk of next-day impairment, including impaired driving, is increased if lemborexant is taken with other CNS depressants. Patients should generally avoid nonprescription antihistamine products that are marketed as sleep-aids concurrently with lemborexant.
Levalbuterol: (Moderate) Caution and close observation should be used when albuterol is used concurrently with other adrenergic sympathomimetics, administered by any route, to avoid potential for increased cardiovascular effects.
Levamlodipine: (Moderate) Phenylephrine's cardiovascular effects may reduce the antihypertensive effects of calcium-channel blockers. Well-controlled hypertensive patients receiving decongestant sympathomimetics at recommended doses do not appear to be at high risk for significant elevations in blood pressure; however, increased blood pressure (especially systolic hypertension) has been reported in some patients.
Levobetaxolol: (Minor) Close monitoring of blood pressure or the selection of alternative therapeutic agents to the sympathomimetic agent may be needed in patients receiving a beta-blocker. Sympathomimetics, such as amphetamines, phentermine, and decongestants (e.g., pseudoephedrine, phenylephrine), and many other drugs, may increase both systolic and diastolic blood pressure and may counteract the activity of the beta-blockers. Concurrent use increases the risk of unopposed alpha-adrenergic activity. Increased blood pressure, bradycardia, or heart block may occur due to excessive alpha-adrenergic receptor stimulation.
Levobunolol: (Minor) Close monitoring of blood pressure or the selection of alternative therapeutic agents to the sympathomimetic agent may be needed in patients receiving a beta-blocker. Sympathomimetics, such as amphetamines, phentermine, and decongestants (e.g., pseudoephedrine, phenylephrine), and many other drugs, may increase both systolic and diastolic blood pressure and may counteract the activity of the beta-blockers. Concurrent use increases the risk of unopposed alpha-adrenergic activity. Increased blood pressure, bradycardia, or heart block may occur due to excessive alpha-adrenergic receptor stimulation.
Levocetirizine: (Moderate) Due to the duplicative and additive pharmacology, concurrent use of cetirizine/levocetirizine with sedating H1-blockers should generally be avoided. Coadministration may increase the risk of anticholinergic and CNS depressant-related side effects. If concurrent use is necessary, monitor for excessive anticholinergic effects, sedation, and somnolence.
Levomethadyl: (Moderate) Enhanced CNS depressant effects may occur when levomethadyl is combined with other CNS depressants, such as sedating H1 blockers.
Levorphanol: (Moderate) Concomitant use of opioid agonists with chlorpheniramine may cause excessive sedation and somnolence. Limit the use of opioid pain medication with chlorpheniramine to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect.
Levothyroxine: (Moderate) Sympathomimetic amines should be used with caution in patients with thyrotoxicosis since these patients are unusually responsive to sympathomimetic amines. Based on the cardiovascular stimulatory effects of sympathomimetic drugs, the concomitant use of sympathomimetics and thyroid hormones can enhance the effects on the cardiovascular system. Patients with coronary artery disease have an increased risk of coronary insufficiency from either agent. Concomitant use of these agents may increase this risk further. In addition, dopamine at a dose of >= 1 mcg/kg/min and dopamine agonists

(e.g., apomorphine, bromocriptine, levodopa, pergolide, pramipexole, ropinirole, rotigotine) may result in a transient reduction in TSH secretion. The reduction in TSH secretion is not sustained; hypothyroidism does not occur.

Levothyroxine; Liothyronine (Porcine): (Moderate) Sympathomimetic amines should be used with caution in patients with thyrotoxicosis since these patients are unusually responsive to sympathomimetic amines. Based on the cardiovascular stimulatory effects of sympathomimetic drugs, the concomitant use of sympathomimetics and thyroid hormones can enhance the effects on the cardiovascular system. Patients with coronary artery disease have an increased risk of coronary insufficiency from either agent. Concomitant use of these agents may increase this risk further. In addition, dopamine at a dose of >= 1 mcg/kg/min and dopamine agonists (e.g., apomorphine, bromocriptine, levodopa, pergolide, pramipexole, ropinirole, rotigotine) may result in a transient reduction in TSH secretion. The reduction in TSH secretion is not sustained; hypothyroidism does not occur.

Levothyroxine; Liothyronine (Synthetic): (Moderate) Sympathomimetic amines should be used with caution in patients with thyrotoxicosis since these patients are unusually responsive to sympathomimetic amines. Based on the cardiovascular stimulatory effects of sympathomimetic drugs, the concomitant use of sympathomimetics and thyroid hormones can enhance the effects on the cardiovascular system. Patients with coronary artery disease have an increased risk of coronary insufficiency from either agent. Concomitant use of these agents may increase this risk further. In addition, dopamine at a dose of >= 1 mcg/kg/min and dopamine agonists (e.g., apomorphine, bromocriptine, levodopa, pergolide, pramipexole, ropinirole, rotigotine) may result in a transient reduction in TSH secretion. The reduction in TSH secretion is not sustained; hypothyroidism does not occur.

Linagliptin; Metformin: (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.

Linezolid: (Major) Linezolid may enhance the hypertensive effect of phenylephrine. Initial doses of phenylephrine, if given by intravenous infusion, should be reduced and subsequent dosing titrated to desired response. Closely monitor blood pressure during coadministration. Linezolid is an antibiotic that is also a weak, reversible nonselective inhibitor of monoamine oxidase (MAO). Therefore, linezolid has the potential for interaction with adrenergic agents, such as phenylephrine.

Liothyronine: (Moderate) Sympathomimetic amines should be used with caution in patients with thyrotoxicosis since these patients are unusually responsive to sympathomimetic amines. Based on the cardiovascular stimulatory effects of sympathomimetic drugs, the concomitant use of sympathomimetics and thyroid hormones can enhance the effects on the cardiovascular system. Patients with coronary artery disease have an increased risk of coronary insufficiency from either agent. Concomitant use of these agents may increase this risk further. In addition, dopamine at a dose of >= 1 mcg/kg/min and dopamine agonists (e.g., apomorphine, bromocriptine, levodopa, pergolide, pramipexole, ropinirole, rotigotine) may result in a transient reduction in TSH secretion. The reduction in TSH secretion is not sustained; hypothyroidism does not occur.

Liraglutide: (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.

Lithium: (Moderate) Because lithium has the potential to impair cognitive and motor skills, caution is advisable during concurrent use of other medications with centrally-acting effects including the sedating antihistamines.

Lixisenatide: (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.

Lofexidine: (Moderate) Monitor for additive sedation during coadministration of lofexidine and chlorpheniramine. Lofexidine can potentiate the effects of CNS depressants. Patients should be advised to avoid driving or performing any other tasks requiring mental alertness until the effects of the combination are known.

Loop diuretics: (Moderate) The cardiovascular effects of sympathomimetics may reduce the antihypertensive effects produced by diuretics. Well-controlled hypertensive patients receiving decongestant sympathomimetics at recommended doses do not appear at high risk for significant elevations in blood pressure, however, increased blood pressure has been reported in some patients.

Loperamide: (Moderate) The plasma concentration of loperamide, a CYP2D6 substrate, may be increased when administered concurrently with chlorpheniramine, a CYP2D6 inhibitor. If these drugs are used together, monitor for loperamide-associated adverse reactions, such as CNS effects and cardiac toxicities (i.e., syncope, ventricular tachycardia, QT prolongation, torsade de pointes, cardiac arrest).

Loperamide; Simethicone: (Moderate) The plasma concentration of loperamide, a CYP2D6 substrate, may be increased when administered concurrently with chlorpheniramine, a CYP2D6 inhibitor. If these drugs are used together, monitor for loperamide-associated adverse reactions, such as CNS effects and cardiac toxicities (i.e., syncope, ventricular tachycardia, QT prolongation, torsade de pointes, cardiac arrest).

Lopinavir; Ritonavir: (Moderate) Concurrent administration of chlorpheniramine with ritonavir may result in elevated plasma concentrations of chlorpheniramine. Chlorpheniramine is metabolized by the hepatic isoenzyme CYP2D6; ritonavir is an inhibitor of this enzyme. Monitor for adverse effects if these drugs are administered together.

Loratadine: (Minor) Although loratadine is considered a 'non-sedating' antihistamine, dose-related sedation has been noted. For this reason, it would be prudent to monitor for drowsiness during concurrent use of loratadine with CNS depressants such as other H1-blockers.

Loratadine; Pseudoephedrine: (Major) Pseudoephedrine can potentiate the effects and increase the toxicity of other sympathomimetics by adding to their sympathomimetic activity. Although no data are available, pseudoephedrine should be used cautiously in patients using significant quantities of other sympathomimetics. (Minor) Although loratadine is considered a 'non-sedating' antihistamine, dose-related sedation has been noted. For this reason, it would be prudent to monitor for drowsiness during concurrent use of loratadine with CNS depressants such as other H1-blockers.

Lorazepam: (Moderate) The therapeutic effect of phenylephrine may be decreased in patients receiving benzodiazepines. Monitor patients for decreased pressor effect if these agents are administered concomitantly.
Loxapine: (Moderate) Patients taking loxapine can have reduced pressor response to phenylephrine. (Moderate) Sedating H1-blockers are associated with anticholinergic effects and sedation; therefore, additive effects may be seen during concurrent use with other drugs having anticholinergic activity and CNS depressant properties such as traditional antipsychotic agents, including loxapine. Clinicians should note that antimuscarinic effects may be seen not only on GI smooth muscle, but also on bladder function, the eye, and temperature regulation. Additive drowsiness or other CNS effects may also occur.
Lumateperone: (Moderate) Monitor for excessive sedation and somnolence during coadministration of lumateperone and chlorpheniramine. Concurrent use may result in additive CNS depression.
Lurasidone: (Moderate) Due to the CNS effects of lurasidone, caution should be used when lurasidone is given in combination with other centrally acting medications. Sedating H1-blockers are associated with sedation; therefore, additive effects may be seen during concurrent use with other drugs having CNS depressant properties such as antipsychotics. Additive drowsiness or other CNS effects may occur.
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.
Magnesium Salts: (Minor) Because of the CNS-depressant effects of magnesium sulfate, additive central-depressant effects can occur following concurrent administration with CNS depressants such as sedating H1-blockers. Caution should be exercised when using these agents concurrently.
Maprotiline: (Moderate) Additive anticholinergic effects may be seen when maprotiline is used concomitantly with other commonly used drugs with moderate to significant anticholinergic effects including sedating h1-blockers. (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: (Major) Meclizine is an H1-blocker which exhibits significant anticholinergic effects. The anticholinergic effects of meclizine may be enhanced when combined with other drugs with antimuscarinic activity, including other sedating H1-blockers. Clinicians should note that antimuscarinic effects might be seen not only on GI smooth muscle, but also on bladder function, the eye, and temperature regulation. Additive sedation may also occur.
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.

Melatonin: (Moderate) Concomitant administration of sedating antihistamines and melatonin may cause additive CNS depression and should be used cautiously in combination. Especially use caution when combining melatonin with sedating antihistamines found in OTC sleep products, since over-sedation, CNS effects, or sleep-related behaviors may occur. Use of more than one agent for hypnotic purposes may increase the risk for over-sedation, CNS effects, or sleep-related behaviors. Be alert for unusual changes in moods or behaviors. Patients reporting unusual sleep-related behaviors likely should discontinue melatonin use.

Meperidine: (Moderate) Concomitant use of opioid agonists with chlorpheniramine may cause excessive sedation and somnolence. Limit the use of opioid pain medication with chlorpheniramine to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect.

Meperidine; Promethazine: (Moderate) Additive anticholinergic and sedative effects may be seen when promethazine is used with first generation antihistamines, such as chlorpheniramine. Patients should be informed to read non-prescription cough and cold product labels carefully for additional interacting antihistamines. (Moderate) Concomitant use of opioid agonists with chlorpheniramine may cause excessive sedation and somnolence. Limit the use of opioid pain medication with chlorpheniramine to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect.

Mephobarbital: (Moderate) Additive CNS depression may occur if barbiturates are co-used with sedating antihistamines, such as chlorpheniramine. Monitor for additive CNS and respiratory effects, and warn about the potential effects to driving and other activities.

Meprobamate: (Moderate) The CNS-depressant effects of meprobamate can be potentiated with concomitant administration of other drugs known to cause CNS depression including sedating H1-blockers.

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.

Metaxalone: (Moderate) Concomitant administration of metaxalone with other CNS depressants can potentiate the sedative effects of either agent.

Metformin: (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.

Metformin; Pioglitazone: (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.

Metformin; 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.

Metformin; Rosiglitazone: (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.

Metformin; Saxagliptin: (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.

Metformin; Sitagliptin: (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.

Methadone: (Moderate) Concomitant use of opioid agonists with chlorpheniramine may cause excessive sedation and somnolence. Limit the use of opioid pain medication with chlorpheniramine to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect.

Methamphetamine: (Moderate) Amphetamines may pharmacodynamically counteract the sedative properties of sedating H1-blockers. 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. Coadminister with caution and monitor for altered response to drug therapy.

Methocarbamol: (Moderate) Methocarbamol may cause additive CNS depression if used concomitantly with other CNS depressants such as sedating H1-blockers. Combination therapy can cause additive effects of sedation and dizziness, which can impair the patient's ability to undertake tasks requiring mental

alertness. Dosage adjustments of either or both medications may be necessary.
Methohexital: (Moderate) Additive CNS depression may occur if barbiturates are co-used with sedating antihistamines, such as chlorpheniramine. Monitor for additive CNS and respiratory effects, and warn about the potential effects to driving and other activities.
Methyclothiazide: (Moderate) The cardiovascular effects of sympathomimetics may reduce the antihypertensive effects produced by diuretics. Well-controlled hypertensive patients receiving decongestant sympathomimetics at recommended doses do not appear at high risk for significant elevations in blood pressure, however, increased blood pressure has been reported in some patients.
Methyldopa: (Major) Sympathomimetics, such as phenylephrine, can antagonize the antihypertensive effects of methyldopa when administered concomitantly. Blood pressure should be monitored closely to confirm that the desired antihypertensive effect is achieved.
Methylergonovine: (Severe) Ergot alkaloids should not be administered with vasoconstrictors such as vasopressors (e.g., norepinephrine, dopamine, phenylephrine) since combining these agents may produce a synergistic increase in blood pressure. There is also an additive risk of peripheral ischemia or gangrene. Of note, at therapeutic doses, ergoloid mesylates lack the vasoconstrictor properties of the natural ergot alkaloids; therefore, ergoloid mesylates are not expected to interact with sympathomimetics.
Methylphenidate: (Moderate) Methylphenidate can potentiate the actions of both exogenous (such as dopamine and epinephrine) and endogenous (such as norepinephrine) vasopressors. It is advisable to monitor cardiac function if these medications are coadministered. Vasopressors include medications such as epinephrine, dopamine, midodrine, and non-prescription medications such as pseudoephedrine and phenylephrine.
Methylprednisolone: (Moderate) The therapeutic effect of phenylephrine may be increased in patient receiving corticosteroids, such as hydrocortisone. Monitor patients for increased pressor effect if these agents are administered concomitantly.
Methysergide: (Severe) Ergot alkaloids should not be administered with vasoconstrictors such as vasopressors (e.g., norepinephrine, dopamine, phenylephrine) since combining these agents may produce a synergistic increase in blood pressure. There is also an additive risk of peripheral ischemia or gangrene. Of note, at therapeutic doses, ergoloid mesylates lack the vasoconstrictor properties of the natural ergot alkaloids; therefore, ergoloid mesylates are not expected to interact with sympathomimetics.
Metoclopramide: (Minor) Combined use of metoclopramide and other CNS depressants, such as anxiolytics, sedatives, and hypnotics, can increase possible sedation.
Metolazone: (Moderate) The cardiovascular effects of sympathomimetics may reduce the antihypertensive effects produced by diuretics. Well-controlled hypertensive patients receiving decongestant sympathomimetics at recommended doses do not appear at high risk for significant elevations in blood pressure, however, increased blood pressure has been reported in some patients.
Metoprolol: (Minor) Close monitoring of blood pressure or the selection of alternative therapeutic agents to the sympathomimetic agent may be needed in patients receiving a beta-blocker. Sympathomimetics, such as amphetamines, phentermine, and decongestants (e.g., pseudoephedrine, phenylephrine), and many other drugs, may increase both systolic and diastolic blood pressure and may counteract the activity of the beta-blockers. Concurrent use increases the risk of unopposed alpha-adrenergic activity. Increased blood pressure, bradycardia, or heart block may occur due to excessive alpha-adrenergic receptor stimulation.
Metyrapone: (Moderate) Metyrapone may cause dizziness and/or drowsiness. Other drugs that may also cause drowsiness, such as sedating H1-blockers, should be used with caution. Additive drowsiness and/or dizziness is possible.
Metyrosine: (Moderate) The concomitant administration of metyrosine with sedating H1-blockers can result in additive sedative effects.

Midazolam: (Moderate) The therapeutic effect of phenylephrine may be decreased in patients receiving benzodiazepines. Monitor patients for decreased pressor effect if these agents are administered concomitantly.
Midodrine: (Major) Midodrine stimulates alpha-adrenergic receptors. Coadministration of midodrine with other vasoconstrictive agents, such as phenylephrine, may enhance or potentiate the effects of midodrine.
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.
Minocycline: (Minor) Injectable minocycline contains magnesium sulfate heptahydrate. Because of the CNS-depressant effects of magnesium sulfate, additive central-depressant effects can occur following concurrent administration with CNS depressants, such as sedating H1-blockers. Caution should be exercised when using these agents concurrently.
Mirabegron: (Moderate) Mirabegron is a moderate CYP2D6 inhibitor. Exposure of drugs metabolized by CYP2D6 isoenzymes such as chlorpheniramine may be increased when co-administered with mirabegron. Therefore, appropriate monitoring and dose adjustment may be necessary.
Mirtazapine: (Moderate) Consistent with the CNS depressant effects of mirtazapine, additive effects may occur with other CNS depressants such as chlorpheniramine. Mirtazapine should be administered cautiously with such agents because the CNS effects on cognitive performance and motor skills can be additive.
Mitotane: (Moderate) Mitotane can cause sedation, lethargy, vertigo, and other CNS side effects. Concomitant administration of mitotane and CNS depressants, including sedating h1-blockers, may cause additive CNS effects.
Molindone: (Moderate) An enhanced CNS depressant effect may occur when sedating h1-blockers are combined with other CNS depressants including molindone.
Mometasone: (Moderate) The therapeutic effect of phenylephrine may be increased in patient receiving corticosteroids, such as hydrocortisone. Monitor patients for increased pressor effect if these agents are administered concomitantly.
Monoamine oxidase inhibitors: (Severe) 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. (Major) Concurrent use of monoamine oxidase inhibitors (MAOIs) and sedating H1-blockers (antihistamines) may result in additive sedation, anticholinergic effects, or hypotensive reactions. Consider alternative therapy to these antihistamines where possible. If alternative combinations are not available, these medications may be used together with close monitoring. Many nonprescription products for coughs, colds, allergy, hay fever, or insomnia contain sedating antihistamines. Patients receiving an MAOI should be counseled that it is essential to consult their health care provider or pharmacist prior to the use of any nonprescription products. Advise against driving or engaging in other activities requiring mental alertness until patients know how this combination affects them.

Morphine: (Moderate) Concomitant use of opioid agonists with chlorpheniramine may cause excessive sedation and somnolence. Limit the use of opioid pain medication with chlorpheniramine to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect.
Morphine; Naltrexone: (Moderate) Concomitant use of opioid agonists with chlorpheniramine may cause excessive sedation and somnolence. Limit the use of opioid pain medication with chlorpheniramine to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect.
Nabilone: (Moderate) Concomitant use of nabilone with other CNS depressants, such as sedating H1-blockers, can potentiate the effects of nabilone on respiratory depression. (Moderate) Concurrent use of nabilone with sympathomimetics (e.g., amphetamine or cocaine) may result in additive hypertension, tachycardia, and possibly cardiotoxicity. In a study of 7 adult males, combinations of cocaine (IV) 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 reaching a plateau at 50 bpm.
Nadolol: (Minor) Close monitoring of blood pressure or the selection of alternative therapeutic agents to the sympathomimetic agent may be needed in patients receiving a beta-blocker. Sympathomimetics, such as amphetamines, phentermine, and decongestants (e.g., pseudoephedrine, phenylephrine), and many other drugs, may increase both systolic and diastolic blood pressure and may counteract the activity of the beta-blockers. Concurrent use increases the risk of unopposed alpha-adrenergic activity. Increased blood pressure, bradycardia, or heart block may occur due to excessive alpha-adrenergic receptor stimulation.
Nafarelin: (Moderate) If use of a topical nasal decongestants (e.g., oxymetazoline, tetrahydrozoline, phenylephrine nasal) is necessary during therapy with intranasal nafarelin, the decongestant should not be used for at least 2 hours after nafarelin is administered.
Nalbuphine: (Moderate) Concomitant use of nalbuphine with other CNS depressants, such as sedating H1-blockers, can potentiate the effects of nalbuphine on respiratory depression, CNS depression, and sedation.
Naproxen; Pseudoephedrine: (Major) Pseudoephedrine can potentiate the effects and increase the toxicity of other sympathomimetics by adding to their sympathomimetic activity. Although no data are available, pseudoephedrine should be used cautiously in patients using significant quantities of other sympathomimetics.
Nebivolol: (Moderate) Monitor for increased toxicity as well as increased therapeutic effect of nebivolol if coadministered with chlorpheniramine. Nebivolol is metabolized by CYP2D6. Although data are lacking, CYP2D6 inhibitors, such as chlorpheniramine, could potentially increase nebivolol plasma concentrations via CYP2D6 inhibition; the clinical significance of this potential interaction is unknown, but an increase in adverse effects is possible. (Minor) Close monitoring of blood pressure or the selection of alternative therapeutic agents to the sympathomimetic agent may be needed in patients receiving a beta-blocker. Sympathomimetics, such as amphetamines, phentermine, and decongestants (e.g., pseudoephedrine, phenylephrine), and many other drugs, may increase both systolic and diastolic blood pressure and may counteract the activity of the beta-blockers. Concurrent use increases the risk of unopposed alpha-adrenergic activity. Increased blood pressure, bradycardia, or heart block may occur due to excessive alpha-adrenergic receptor stimulation.
Nebivolol; Valsartan: (Moderate) Monitor for increased toxicity as well as increased therapeutic effect of nebivolol if coadministered with chlorpheniramine. Nebivolol is metabolized by CYP2D6. Although data are lacking, CYP2D6 inhibitors, such as chlorpheniramine, could potentially increase nebivolol plasma concentrations via CYP2D6 inhibition; the clinical significance of this potential interaction is unknown, but an increase in adverse effects is possible. (Minor) Close monitoring of blood pressure or the selection

of alternative therapeutic agents to the sympathomimetic agent may be needed in patients receiving a beta-blocker. Sympathomimetics, such as amphetamines, phentermine, and decongestants (e.g., pseudoephedrine, phenylephrine), and many other drugs, may increase both systolic and diastolic blood pressure and may counteract the activity of the beta-blockers. Concurrent use increases the risk of unopposed alpha-adrenergic activity. Increased blood pressure, bradycardia, or heart block may occur due to excessive alpha-adrenergic receptor stimulation.

Nefazodone: (Moderate) An enhanced CNS depressant effect may occur when sedating H1-blockers are combined with other CNS depressants including nefazodone.

Nicardipine: (Moderate) Phenylephrine's cardiovascular effects may reduce the antihypertensive effects of calcium-channel blockers. Well-controlled hypertensive patients receiving decongestant sympathomimetics at recommended doses do not appear to be at high risk for significant elevations in blood pressure; however, increased blood pressure (especially systolic hypertension) has been reported in some patients.

Nicotine: (Minor) Vasoconstricting nasal decongestants such as oxymetazoline, phenylephrine, pseudoephedrine, and tetrahydrozoline prolong the time to peak effect of nasally administered nicotine (i.e. nicotine nasal spray); however, no dosage adjustments are recommended.

Nifedipine: (Moderate) Phenylephrine's cardiovascular effects may reduce the antihypertensive effects of calcium-channel blockers. Well-controlled hypertensive patients receiving decongestant sympathomimetics at recommended doses do not appear to be at high risk for significant elevations in blood pressure; however, increased blood pressure (especially systolic hypertension) has been reported in some patients.

Nimodipine: (Moderate) Phenylephrine's cardiovascular effects may reduce the antihypertensive effects of calcium-channel blockers. Well-controlled hypertensive patients receiving decongestant sympathomimetics at recommended doses do not appear to be at high risk for significant elevations in blood pressure; however, increased blood pressure (especially systolic hypertension) has been reported in some patients.

Nisoldipine: (Moderate) Phenylephrine's cardiovascular effects may reduce the antihypertensive effects of calcium-channel blockers. Well-controlled hypertensive patients receiving decongestant sympathomimetics at recommended doses do not appear to be at high risk for significant elevations in blood pressure; however, increased blood pressure (especially systolic hypertension) has been reported in some patients.

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.

Non-Ionic Contrast Media: (Major) Do not administer non-ionic contrast media intra-arterially after the administration of vasopressors since they strongly potentiate neurologic effects.

Olanzapine: (Moderate) Olanzapine exhibits anticholinergic effects that may be clinically significant. Clinicians should keep this in mind when using antimuscarinics and other medications with anticholinergic activity in combination with olanzapine. Some medications exhibit additive anticholinergic effects include sedating H1-blockers. Olanzapine may also cause additive sedation with many of these drugs.

Oliceridine: (Moderate) Concomitant use of opioid agonists with chlorpheniramine may cause excessive sedation and somnolence. Limit the use of opioid pain medication with chlorpheniramine to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect.

Ombitasvir; Paritaprevir; Ritonavir: (Moderate) Concurrent administration of chlorpheniramine with ritonavir may result in elevated plasma concentrations of chlorpheniramine. Chlorpheniramine is

metabolized by the hepatic isoenzyme CYP2D6; ritonavir is an inhibitor of this enzyme. Monitor for adverse effects if these drugs are administered together.

Opiate Agonists: (Moderate) Concomitant use of opioid agonists with chlorpheniramine may cause excessive sedation and somnolence. Limit the use of opioid pain medication with chlorpheniramine to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect.

Opicapone: (Moderate) COMT inhibitors should be given cautiously with other agents that cause CNS depression, including sedating H1-blockers, due to the possibility of additive sedation. COMT inhibitors have also been associated with sudden sleep onset during activities of daily living such as driving, which has resulted in accidents in some cases. Prescribers should re-assess patients for drowsiness or sleepiness regularly throughout treatment, especially since events may occur well after the start of treatment. Patients should be advised to avoid driving or other tasks requiring mental alertness until they know how the combination affects them.

Oritavancin: (Moderate) Chlorpheniramine is metabolized by CYP2D6; oritavancin is a weak CYP2D6 inducer. Plasma concentrations and efficacy of chlorpheniramine may be reduced if these drugs are administered concurrently.

Orphenadrine: (Moderate) Additive anticholinergic effects may be seen when drugs with anticholinergic properties, like sedating H1-blockers and orphenadrine, are used concomitantly. Adverse effects may be seen not only on GI smooth muscle, but also on bladder function, the CNS, the eye, and temperature regulation. Additive drowsiness may also occur.

Oxazepam: (Moderate) The therapeutic effect of phenylephrine may be decreased in patients receiving benzodiazepines. Monitor patients for decreased pressor effect if these agents are administered concomitantly.

Oxycodone: (Moderate) Concomitant use of opioid agonists with chlorpheniramine may cause excessive sedation and somnolence. Limit the use of opioid pain medication with chlorpheniramine to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect.

Oxymorphone: (Moderate) Concomitant use of opioid agonists with chlorpheniramine may cause excessive sedation and somnolence. Limit the use of opioid pain medication with chlorpheniramine to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect.

Oxytocin: (Major) The administration of prophylactic vasopressors with oxytocin can cause severe, persistent hypertension, as the 2 drugs may have a synergistic and additive vasoconstrictive effect. This interaction was noted when oxytocin was given 3 to 4 hours after prophylactic vasoconstrictor in conjunction with caudal anesthesia. The incidence of such an interaction may be decreased if vasopressors are not administered prior to oxytocin.

Ozanimod: (Major) Coadministration of ozanimod with sympathomimetics such as phenylephrine is not routinely recommended due to the potential for hypertensive crisis. If coadministration is medically necessary, closely monitor the patient for hypertension. An active metabolite of ozanimod inhibits MAO-B, which may increase the potential for hypertensive crisis. Sympathomimetics may increase blood pressure by increasing norepinephrine concentrations and monoamine oxidase inhibitors (MAOIs) are known to potentiate these effects. Concomitant use of ozanimod with pseudoephedrine did not potentiate the effects on blood pressure. However, hypertensive crisis has occurred with administration of ozanimod alone and also during coadministration of sympathomimetic medications and other selective or nonselective MAO inhibitors.

Paliperidone: (Moderate) Coadministration of drugs with CNS depressant effects, including paliperidone

and chlorpheniramine, can increase both the frequency and the intensity of adverse effects such as drowsiness, sedation, and dizziness. Monitor for signs and symptoms of CNS depression and advise patients to avoid driving or engaging in other activities requiring mental alertness until they know how this combination affects them.

Paromomycin: (Minor) Chlorpheniramine may effectively mask vestibular symptoms (e.g. dizziness, tinnitus, or vertigo) that are associated with ototoxicity induced by aminoglycosides. Antiemetics block the histamine or acetylcholine response that causes nausea due to vestibular emetic stimuli such as motion.

Paroxetine: (Moderate) Of the selective serotonin reuptake inhibiting antidepressants (SSRIs), paroxetine is considered the most anticholinergic. Additive anticholinergic effects may be seen when paroxetine is used with antihistamines having anticholinergic properties such as chlorpheniramine. Patients should be informed to read non-prescription cough and cold product labels carefully for additional interacting antihistamines.

Peginterferon Alfa-2b: (Moderate) Monitor for adverse effects associated with increased exposure to chlorpheniramine if peginterferon alfa-2b is coadministered. Peginterferon alfa-2b is a CYP2D6 inhibitor, while chlorpheniramine is a CYP2D6 substrate.

Penbutolol: (Minor) Close monitoring of blood pressure or the selection of alternative therapeutic agents to the sympathomimetic agent may be needed in patients receiving a beta-blocker. Sympathomimetics, such as amphetamines, phentermine, and decongestants (e.g., pseudoephedrine, phenylephrine), and many other drugs, may increase both systolic and diastolic blood pressure and may counteract the activity of the beta-blockers. Concurrent use increases the risk of unopposed alpha-adrenergic activity. Increased blood pressure, bradycardia, or heart block may occur due to excessive alpha-adrenergic receptor stimulation.

Pentazocine: (Moderate) Use pentazocine with caution in any patient receiving medication with CNS depressant and/or anticholinergic activity. Coadministration of pentazocine with sedating H1-blockers may result in additive respiratory and CNS depression and anticholinergic effects, such as urinary retention and constipation.

Pentazocine; Naloxone: (Moderate) Use pentazocine with caution in any patient receiving medication with CNS depressant and/or anticholinergic activity. Coadministration of pentazocine with sedating H1-blockers may result in additive respiratory and CNS depression and anticholinergic effects, such as urinary retention and constipation.

Pentobarbital: (Moderate) Additive CNS depression may occur if barbiturates are co-used with sedating antihistamines, such as chlorpheniramine. Monitor for additive CNS and respiratory effects, and warn about the potential effects to driving and other activities.

Perampanel: (Moderate) Co-administration of perampanel with CNS depressants, including ethanol, may increase CNS depression. The combination of perampanel (particularly at high doses) with ethanol has led to decreased mental alertness and ability to perform complex tasks (such as driving), as well as increased levels of anger, confusion, and depression; similar reactions should be expected with concomitant use of other CNS depressants, such as sedating H1-blockers.

Pergolide: (Severe) Ergot alkaloids should not be administered with vasoconstrictors such as vasopressors (e.g., norepinephrine, dopamine, phenylephrine) since combining these agents may produce a synergistic increase in blood pressure. There is also an additive risk of peripheral ischemia or gangrene. Of note, at therapeutic doses, ergoloid mesylates lack the vasoconstrictor properties of the natural ergot alkaloids; therefore, ergoloid mesylates are not expected to interact with sympathomimetics.

Perindopril; Amlodipine: (Moderate) Phenylephrine's cardiovascular effects may reduce the antihypertensive effects of calcium-channel blockers. Well-controlled hypertensive patients receiving decongestant sympathomimetics at recommended doses do not appear to be at high risk for significant elevations in blood pressure; however, increased blood pressure (especially systolic hypertension) has been

reported in some patients.
Perphenazine: (Moderate) Additive anticholinergic and sedative effects may be seen when perphenazine is used with first generation antihistamines, such as chlorpheniramine. Patients should be informed to read non-prescription cough and cold product labels carefully for additional interacting antihistamines.
Perphenazine; Amitriptyline: (Moderate) Additive anticholinergic and sedative effects may be seen when perphenazine is used with first generation antihistamines, such as chlorpheniramine. Patients should be informed to read non-prescription cough and cold product labels carefully for additional interacting antihistamines.
Phendimetrazine: (Major) Phendimetrazine is a phenylalkaline sympathomimetic agent. All sympathomimetics and psychostimulants, including other anorexiants, should be used cautiously or avoided in patients receiving phendimetrazine. The combined use of these agents may have the potential for additive side effects, such as hypertensive crisis or cardiac arrhythmia.
Phenelzine: (Severe) 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. (Major) Concurrent use of monoamine oxidase inhibitors (MAOIs) and sedating H1-blockers (antihistamines) may result in additive sedation, anticholinergic effects, or hypotensive reactions. Consider alternative therapy to these antihistamines where possible. If alternative combinations are not available, these medications may be used together with close monitoring. Many nonprescription products for coughs, colds, allergy, hay fever, or insomnia contain sedating antihistamines. Patients receiving an MAOI should be counseled that it is essential to consult their health care provider or pharmacist prior to the use of any nonprescription products. Advise against driving or engaging in other activities requiring mental alertness until patients know how this combination affects them.
Phenobarbital: (Moderate) Additive CNS depression may occur if barbiturates are co-used with sedating antihistamines, such as chlorpheniramine. Monitor for additive CNS and respiratory effects, and warn about the potential effects to driving and other activities.
Phenothiazines: (Moderate) Other non-cardiovascular drugs with alpha-blocking activity such as phenothiazines, directly counteract the effects of phenylephrine and can counter the desired pharmacologic effect. They also can be used to treat excessive phenylephrine-induced hypertension.
Phenoxybenzamine: (Major) Sympathomimetics can antagonize the effects of antihypertensives such as alpha-blockers when administered concomitantly.
Phentermine: (Major) Because phentermine is a sympathomimetic and anorexic agent (i.e., psychostimulant) it should not be used in combination with other sympathomimetics. The combined use of these agents may have the potential for additive side effects, such as hypertensive crisis or cardiac arrhythmias.
Phentermine; Topiramate: (Major) Because phentermine is a sympathomimetic and anorexic agent (i.e., psychostimulant) it should not be used in combination with other sympathomimetics. The combined use of these agents may have the potential for additive side effects, such as hypertensive crisis or cardiac arrhythmias.
Phentolamine: (Major) Sympathomimetics can antagonize the effects of antihypertensives such as alpha-blockers when administered concomitantly.
Phenylephrine; Promethazine: (Moderate) Additive anticholinergic and sedative effects may be seen when promethazine is used with first generation antihistamines, such as chlorpheniramine. Patients should

be informed to read non-prescription cough and cold product labels carefully for additional interacting antihistamines.

Phosphodiesterase inhibitors: (Minor) The therapeutic effect of phenylephrine injection may be decreased in patients receiving phosphodiesterase inhibitors. A decreased pressor effect of phenylephrine might occur. Monitor for proper blood pressure when these drugs are used together,

Pimozide: (Moderate) Due to the effects of pimozide on cognition, it should be used cautiously with other CNS depressants including sedating antihistamines. Sedating H1-blockers are associated with anticholinergic effects and sedation; therefore, additive effects may be seen during concurrent use with pimozide. Additive drowsiness or other CNS effects may occur.

Pindolol: (Minor) Close monitoring of blood pressure or the selection of alternative therapeutic agents to the sympathomimetic agent may be needed in patients receiving a beta-blocker. Sympathomimetics, such as amphetamines, phentermine, and decongestants (e.g., pseudoephedrine, phenylephrine), and many other drugs, may increase both systolic and diastolic blood pressure and may counteract the activity of the beta-blockers. Concurrent use increases the risk of unopposed alpha-adrenergic activity. Increased blood pressure, bradycardia, or heart block may occur due to excessive alpha-adrenergic receptor stimulation.

Pioglitazone: (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.

Pirbuterol: (Moderate) Caution and close observation should also be used when pirbuterol is used concurrently with other adrenergic sympathomimetics, administered by any route, to avoid potential for increased cardiovascular effects.

Pitolisant: (Major) Avoid coadministration of pitolisant with chlorpheniramine as the effect of pitolisant may be decreased. Pitolisant increases histamine concentrations in the brain; therefore, H1-receptor antagonists like chlorpheniramine, may reduce pitolisant efficacy.

Plazomicin: (Minor) Chlorpheniramine may effectively mask vestibular symptoms (e.g. dizziness, tinnitus, or vertigo) that are associated with ototoxicity induced by aminoglycosides. Antiemetics block the histamine or acetylcholine response that causes nausea due to vestibular emetic stimuli such as motion.

Potassium-sparing diuretics: (Moderate) The cardiovascular effects of sympathomimetics may reduce the antihypertensive effects produced by diuretics. Well-controlled hypertensive patients receiving decongestant sympathomimetics at recommended doses do not appear at high risk for significant elevations in blood pressure, however, increased blood pressure has been reported in some patients.

Pramipexole: (Moderate) Concomitant use of pramipexole with other CNS depressants, such as sedating H1-blockers, can potentiate the sedation effects of pramipexole.

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: (Major) Sympathomimetics can antagonize the effects of antihypertensives such as alpha-blockers when administered concomitantly.
Prednisolone: (Moderate) The therapeutic effect of phenylephrine may be increased in patient receiving corticosteroids, such as hydrocortisone. Monitor patients for increased pressor effect if these agents are administered concomitantly.
Prednisone: (Moderate) The therapeutic effect of phenylephrine may be increased in patient receiving corticosteroids, such as hydrocortisone. Monitor patients for increased pressor effect if these agents are administered concomitantly.
Pregabalin: (Moderate) Monitor for excessive sedation and somnolence during coadministration of chlorpheniramine and pregabalin. Concurrent use may result in additive CNS depression.
Prilocaine; Epinephrine: (Major) Because epinephrine is a sympathomimetic drug with agonist actions at both the alpha and beta receptors, caution is warranted in patients receiving epinephrine concomitantly with other sympathomimetics as additive pharmacodynamic effects are possible, some which may be undesirable.
Primidone: (Moderate) Additive CNS depression may occur if barbiturates are co-used with sedating antihistamines, such as chlorpheniramine. Monitor for additive CNS and respiratory effects, and warn about the potential effects to driving and other activities.
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. (Moderate) Use procarbazine and sedating H1-blockers together with caution; additive central nervous system depression may occur.
Prochlorperazine: (Moderate) Additive anticholinergic and sedative effects may be seen when prochlorperazine is used with first generation antihistamines, such as chlorpheniramine. Patients should be informed to read non-prescription cough and cold product labels carefully for additional interacting antihistamines.
Promethazine: (Moderate) Additive anticholinergic and sedative effects may be seen when promethazine is used with first generation antihistamines, such as chlorpheniramine. Patients should be informed to read non-prescription cough and cold product labels carefully for additional interacting antihistamines.
Propofol: (Moderate) Initially, vasopressors may reduce propofol serum concentrations due to increased metabolic clearance secondary to increased hepatic blood flow. An increase in the propofol dose may be required. Additionally, the vasopressor dose may need to be increased over time due to tachyphylaxis. Thus, these drugs may drive each other in a progressively myocardial depressive loop, which could lead to cardiac arrhythmias or cardiac failure. (Minor) Because sedating H1-blockers cause sedation, an enhanced CNS depressant effect may occur when they are combined with general anesthetics.
Propoxyphene: (Moderate) Concomitant use of opioid agonists with chlorpheniramine may cause excessive sedation and somnolence. Limit the use of opioid pain medication with chlorpheniramine to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect.
Propranolol: (Minor) Close monitoring of blood pressure or the selection of alternative therapeutic agents

to the sympathomimetic agent may be needed in patients receiving a beta-blocker. Sympathomimetics, such as amphetamines, phentermine, and decongestants (e.g., pseudoephedrine, phenylephrine), and many other drugs, may increase both systolic and diastolic blood pressure and may counteract the activity of the beta-blockers. Concurrent use increases the risk of unopposed alpha-adrenergic activity. Increased blood pressure, bradycardia, or heart block may occur due to excessive alpha-adrenergic receptor stimulation.
Pseudoephedrine: (Major) Pseudoephedrine can potentiate the effects and increase the toxicity of other sympathomimetics by adding to their sympathomimetic activity. Although no data are available, pseudoephedrine should be used cautiously in patients using significant quantities of other sympathomimetics.
Quazepam: (Moderate) The therapeutic effect of phenylephrine may be decreased in patients receiving benzodiazepines. Monitor patients for decreased pressor effect if these agents are administered concomitantly.
Quetiapine: (Moderate) Somnolence is a commonly reported adverse effect of quetiapine. Co-administration of quetiapine with sedating H1-blockers may result in additive effects. Additive drowsiness or other CNS effects may occur.
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.
Ramelteon: (Moderate) Because sedating H1-blockers cause sedation, an enhanced CNS depressant effect may occur when it is combined with other CNS depressants including anxiolytics, sedatives, and hypnotics, such as ramelteon.
Rasagiline: (Moderate) Concurrent use of monoamine oxidase inhibitors (MAOIs) and sedating H1-blockers (sedating antihistamines) may result in additive sedation, anticholinergic effects, or hypotensive reactions. Rasagiline may be less likely to produce these interactions than other MAOIs, due to MAO-B selectivity. However, consider alternatives therapy to antihistamines where possible. If alternative combinations are not available, these medications may be used together with close monitoring. Many non-prescription products for coughs, colds, allergy, hay fever or insomnia contain sedating antihistamines. Patients receiving rasagiline should be counseled that it is essential to consult their healthcare provider or pharmacist prior to the use of any non-prescription products. Patients should also be advised against driving or engaging in other activities requiring mental alertness until they know how this combination affects them. (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.

Remifentanil: (Moderate) Concomitant use of opioid agonists with chlorpheniramine may cause excessive sedation and somnolence. Limit the use of opioid pain medication with chlorpheniramine to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect.

Reserpine: (Major) The cardiovascular effects of sympathomimetics, such as phenylephrine, may reduce the antihypertensive effects produced by reserpine. Blood pressure and heart rates should be monitored closely to confirm that the desired antihypertensive effect is achieved.

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.

Risperidone: (Moderate) Due to the primary CNS effects of risperidone, caution is advisable when risperidone is given with other centrally acting medications including sedating H1-blockers such as chlorpheniramine. Patients should be informed of the risk of driving or performing other tasks requiring mental alertness until the effects of these medicines are known.

Ritonavir: (Moderate) Concurrent administration of chlorpheniramine with ritonavir may result in elevated plasma concentrations of chlorpheniramine. Chlorpheniramine is metabolized by the hepatic isoenzyme CYP2D6; ritonavir is an inhibitor of this enzyme. Monitor for adverse effects if these drugs are administered together.

Rituximab; Hyaluronidase: (Minor) H1-blockers (antihistamines), when given in large systemic doses, may render tissues partially resistant to the action of hyaluronidase. Patients receiving these medications may require larger amounts of hyaluronidase for equivalent dispersing effect.

Rivastigmine: (Moderate) Concurrent use of sedating H1-blockers and rivastigmine should be avoided if possible. Rivastigmine inhibits acetylcholinesterase, the enzyme responsible for the degradation of acetylcholine, and improves the availability of acetylcholine. Sedating H1-blockers may exhibit significant anticholinergic activity, thereby interfering with the therapeutic effect of rivastigmine.

Rolapitant: (Major) Use caution if products containing chlorpheniramine and rolapitant are used concurrently, and monitor for chlorpheniramine-related adverse effects. Consider if another antihistamine would be a better choice for treatment. Chlorpheniramine is a CYP2D6 substrate and rolapitant is a moderate CYP2D6 inhibitor; the inhibitory effect of rolapitant is expected to persist beyond 28 days for an unknown duration. Exposure to another CYP2D6 substrate, following a single dose of rolapitant increased about 3-fold on Days 8 and Day 22. The inhibition of CYP2D6 persisted on Day 28 with a 2.3-fold increase in the CYP2D6 substrate concentrations, the last time point measured.

Ropinirole: (Moderate) Concomitant use of ropinirole with other CNS depressants, such as sedating H1-blockers, can potentiate the sedation effects of ropinirole.

Rosiglitazone: (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.

Safinamide: (Moderate) Dopaminergic medications, including safinamide, may cause a sudden onset of somnolence which sometimes has resulted in motor vehicle accidents. Patients may not perceive warning signs, such as excessive drowsiness, or they may report feeling alert immediately prior to the event. Because of possible additive effects, advise patients about the potential for increased somnolence during concurrent use of other sedating medications, such as sedating H1-blockers. (Moderate) Severe hypertensive reactions, including hypertensive crisis, have been reported in patients taking monoamine oxidase inhibitors (MAOIs), such as safinamide, and sympathomimetic medications, such as phenylephrine. If concomitant use of safinamide and phenylephrine is necessary, monitor for hypertension and hypertensive crisis.

Salmeterol: (Moderate) Caution and close observation should also be used when salmeterol is used concurrently with other adrenergic sympathomimetics, administered by any route, to avoid potential for increased cardiovascular effects.

Secobarbital: (Moderate) Additive CNS depression may occur if barbiturates are co-used with sedating antihistamines, such as chlorpheniramine. Monitor for additive CNS and respiratory effects, and warn about the potential effects to driving and other activities.

Selegiline: (Severe) The product label for phenylephrine contraindicates use with monoamine oxidase inhibitors (MAOIs) due to the risk of hypertensive crisis. Selegiline is a selective monoamine oxidase inhibitor type B; however, the selectivity of the drug decreases with increasing doses. The manufacturers of selegiline products recommend caution and monitoring of blood pressure during concurrent use with sympathomimetics. Phenylephrine should generally not be used concurrently with MAOIs or within 14 days before or after their use. (Moderate) Monitor for excessive sedation and somnolence during coadministration of selegiline and chlorpheniramine. Concurrent use may result in additive CNS depression.

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 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.

Sevoflurane: (Major) Halogenated anesthetics may sensitize the myocardium to the effects of sympathomimetics, including phenylephrine, which can increase the risk of developing cardiac arrhythmias and hypotension.

SGLT2 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.
Sibutramine: (Major) Concurrent use of sibutramine with other serotonergic agents may increase the potential for serotonin syndrome or neuroleptic malignant syndrome-like reactions. Serotonin syndrome is characterized by rapid development of hyperthermia, hypertension, myoclonus, rigidity, autonomic instability, mental status changes (e.g., delirium or coma), and in rare cases, death. Serotonin syndrome, in its most severe form, can resemble neuroleptic malignant syndrome.
Sildenafil: (Minor) The therapeutic effect of phenylephrine injection may be decreased in patients receiving phosphodiesterase inhibitors. A decreased pressor effect of phenylephrine might occur. Monitor for proper blood pressure when these drugs are used together,
Sincalide: (Moderate) Sincalide-induced gallbladder ejection fraction may be affected by concurrent medications, including H1-blockers. False study results are possible; thorough patient history is important in the interpretation of procedure results.
Sodium Iodide: (Moderate) Antihistamines may alter sodium iodide I-131 pharmacokinetics and dynamics for up to 1 week after administration. In addition, medications that decrease salivation increase the time of radiation exposure to salivary glands. Consider discontinuing sedating H1-blockers prior to sodium iodide I-131 administration.
Sodium Sulfate; Magnesium Sulfate; Potassium Chloride: (Minor) Because of the CNS-depressant effects of magnesium sulfate, additive central-depressant effects can occur following concurrent administration with CNS depressants such as sedating H1-blockers. Caution should be exercised when using these agents concurrently.
Solifenacin: (Moderate) Depending on the specific agent, additive anticholinergic effects may be seen when drugs with antimuscarinic properties like solifenacin are used concomitantly with other antimuscarinics, such as sedating H1 blockers.
Solriamfetol: (Moderate) Monitor blood pressure and heart rate during coadministration of solriamfetol, a norepinephrine and dopamine reuptake inhibitor, and vasopressors. 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.
Sotalol: (Minor) Close monitoring of blood pressure or the selection of alternative therapeutic agents to the sympathomimetic agent may be needed in patients receiving a beta-blocker. Sympathomimetics, such as amphetamines, phentermine, and decongestants (e.g., pseudoephedrine, phenylephrine), and many other drugs, may increase both systolic and diastolic blood pressure and may counteract the activity of the beta-blockers. Concurrent use increases the risk of unopposed alpha-adrenergic activity. Increased blood pressure, bradycardia, or heart block may occur due to excessive alpha-adrenergic receptor stimulation.
Spironolactone: (Moderate) The cardiovascular effects of sympathomimetics may reduce the antihypertensive effects produced by diuretics. Well-controlled hypertensive patients receiving decongestant sympathomimetics at recommended doses do not appear at high risk for significant elevations in blood pressure, however, increased blood pressure has been reported in some patients.
St. John's Wort, Hypericum perforatum: (Major) St. John's wort may have MAOI-like activities, and

could potentially increase the cardiac stimulation and vasopressor effects of the sympathomimetics. St. John's wort should be used cautiously with any sympathomimetic agent.
Streptomycin: (Minor) Chlorpheniramine may effectively mask vestibular symptoms (e.g. dizziness, tinnitus, or vertigo) that are associated with ototoxicity induced by aminoglycosides. Antiemetics block the histamine or acetylcholine response that causes nausea due to vestibular emetic stimuli such as motion.
Sufentanil: (Moderate) Concomitant use of opioid agonists with chlorpheniramine may cause excessive sedation and somnolence. Limit the use of opioid pain medication with chlorpheniramine to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect.
Sulfonylureas: (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.
Suvorexant: (Moderate) Monitor for excessive sedation and somnolence during coadministration of suvorexant and sedating antihistamines (H1-blockers). Dosage adjustments of suvorexant and sedating H1-blockers may be necessary when administered together because of potentially additive CNS effects. The risk of next-day impairment, including impaired driving, is increased if suvorexant is taken with other CNS depressants. Patients should generally avoid nonprescription antihistamine products that are marketed as sleep-aids concurrently with suvorexant.
Tacrine: (Moderate) Concurrent use of sedating H1-blockers and tacrine should be avoided if possible. Tacrine inhibits acetylcholinesterase, the enzyme responsible for the degradation of acetylcholine, and improves the availability of acetylcholine. Sedating H1-blockers may exhibit significant anticholinergic activity, thereby interfering with the therapeutic effect of tacrine.
Tadalafil: (Minor) The therapeutic effect of phenylephrine injection may be decreased in patients receiving phosphodiesterase inhibitors. A decreased pressor effect of phenylephrine might occur. Monitor for proper blood pressure when these drugs are used together,
Tamsulosin: (Moderate) Use caution when administering tamsulosin with a moderate CYP2D6 inhibitor such as chlorpheniramine. Tamsulosin is extensively metabolized by CYP2D6 hepatic enzymes. In clinical evaluation, concomitant treatment with a strong CYP2D6 inhibitor resulted in increases in tamsulosin exposure; interactions with moderate CYP2D6 inhibitors have not been evaluated. If concomitant use in necessary, monitor patient closely for increased side effects.
Tapentadol: (Moderate) Concomitant use of opioid agonists with chlorpheniramine may cause excessive sedation and somnolence. Limit the use of opioid pain medication with chlorpheniramine to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect.
Tasimelteon: (Moderate) Because sedating H1-blockers cause sedation, an enhanced CNS depressant effect may occur when it is combined with other CNS depressants including anxiolytics, sedatives, and hypnotics, such as tasimelteon.
Temazepam: (Moderate) The therapeutic effect of phenylephrine may be decreased in patients receiving benzodiazepines. Monitor patients for decreased pressor effect if these agents are administered concomitantly.
Terazosin: (Major) Sympathomimetics can antagonize the effects of antihypertensives such as alpha-

blockers when administered concomitantly.
Terbutaline: (Major) Concomitant use of sympathomimetics with beta-agonists might result in additive cardiovascular effects such as increased blood pressure and heart rate.
Thalidomide: (Major) Avoid the concomitant use of thalidomide with opiate agonists; antihistamines; antipsychotics; anxiolytics, sedatives, and hypnotics; and other central nervous system depressants due to the potential for additive sedative effects.
Theophylline, Aminophylline: (Moderate) Concurrent administration of theophylline or aminophylline with some sympathomimetics can produce excessive stimulation and effects such as nervousness, irritability, or insomnia. (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.
Thiazide diuretics: (Moderate) The cardiovascular effects of sympathomimetics may reduce the antihypertensive effects produced by diuretics. Well-controlled hypertensive patients receiving decongestant sympathomimetics at recommended doses do not appear at high risk for significant elevations in blood pressure, however, increased blood pressure has been reported in some patients.
Thiazolidinediones: (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.
Thiopental: (Moderate) Additive CNS depression may occur if barbiturates are co-used with sedating antihistamines, such as chlorpheniramine. Monitor for additive CNS and respiratory effects, and warn about the potential effects to driving and other activities.
Thioridazine: (Moderate) Additive anticholinergic and sedative effects may be seen when thioridazine is used with first generation antihistamines, such as chlorpheniramine. Patients should be informed to read non-prescription cough and cold product labels carefully for additional interacting antihistamines.
Thiothixene: (Moderate) Additive anticholinergic effects may be seen when antipsychotics, such as thiothixene, are used concomitantly with other drugs such as sedating H1-blockers. Additive drowsiness or other CNS effects may also occur. (Moderate) The alpha-adrenergic effects of epinephrine can be blocked during concurrent administration of thiothixene. This blockade can cause an apparently paradoxical condition called epinephrine reversal, which can lead to severe hypotension, tachycardia, and, potentially, myocardial infarction. Patients taking thiothixene can have reduced pressor response to phenylephrine.
Thyroid hormones: (Moderate) Sympathomimetic amines should be used with caution in patients with thyrotoxicosis since these patients are unusually responsive to sympathomimetic amines. Based on the cardiovascular stimulatory effects of sympathomimetic drugs, the concomitant use of sympathomimetics and thyroid hormones can enhance the effects on the cardiovascular system. Patients with coronary artery disease have an increased risk of coronary insufficiency from either agent. Concomitant use of these agents may increase this risk further. In addition, dopamine at a dose of >= 1 mcg/kg/min and dopamine agonists (e.g., apomorphine, bromocriptine, levodopa, pergolide, pramipexole, ropinirole, rotigotine) may result in a transient reduction in TSH secretion. The reduction in TSH secretion is not sustained; hypothyroidism does not occur.
Timolol: (Minor) Close monitoring of blood pressure or the selection of alternative therapeutic agents to the sympathomimetic agent may be needed in patients receiving a beta-blocker. Sympathomimetics, such

as amphetamines, phentermine, and decongestants (e.g., pseudoephedrine, phenylephrine), and many other drugs, may increase both systolic and diastolic blood pressure and may counteract the activity of the beta-blockers. Concurrent use increases the risk of unopposed alpha-adrenergic activity. Increased blood pressure, bradycardia, or heart block may occur due to excessive alpha-adrenergic receptor stimulation.
Tizanidine: (Moderate) Concurrent use of tizanidine and CNS depressants like sedating h1-blockers can cause additive CNS depression.
Tobramycin: (Minor) Chlorpheniramine may effectively mask vestibular symptoms (e.g. dizziness, tinnitus, or vertigo) that are associated with ototoxicity induced by aminoglycosides. Antiemetics block the histamine or acetylcholine response that causes nausea due to vestibular emetic stimuli such as motion.
Tolcapone: (Moderate) COMT inhibitors should be given cautiously with other agents that cause CNS depression, including sedating H1-blockers, due to the possibility of additive sedation. COMT inhibitors have also been associated with sudden sleep onset during activities of daily living such as driving, which has resulted in accidents in some cases. Prescribers should re-assess patients for drowsiness or sleepiness regularly throughout treatment, especially since events may occur well after the start of treatment. Patients should be advised to avoid driving or other tasks requiring mental alertness until they know how the combination affects them.
Torsemide: (Moderate) The cardiovascular effects of sympathomimetics may reduce the antihypertensive effects produced by diuretics. Well-controlled hypertensive patients receiving decongestant sympathomimetics at recommended doses do not appear at high risk for significant elevations in blood pressure, however, increased blood pressure has been reported in some patients.
Tramadol: (Moderate) Concomitant use of opioid agonists with chlorpheniramine may cause excessive sedation and somnolence. Limit the use of opioid pain medication with chlorpheniramine to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect.
Trandolapril; Verapamil: (Moderate) Phenylephrine's cardiovascular effects may reduce the antihypertensive effects of calcium-channel blockers. Well-controlled hypertensive patients receiving decongestant sympathomimetics at recommended doses do not appear to be at high risk for significant elevations in blood pressure; however, increased blood pressure (especially systolic hypertension) has been reported in some patients.
Tranylcypromine: (Severe) 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. (Major) Concurrent use of monoamine oxidase inhibitors (MAOIs) and sedating H1-blockers (antihistamines) may result in additive sedation, anticholinergic effects, or hypotensive reactions. Consider alternative therapy to these antihistamines where possible. If alternative combinations are not available, these medications may be used together with close monitoring. Many nonprescription products for coughs, colds, allergy, hay fever, or insomnia contain sedating antihistamines. Patients receiving an MAOI should be counseled that it is essential to consult their health care provider or pharmacist prior to the use of any nonprescription products. Advise against driving or engaging in other activities requiring mental alertness until patients know how this combination affects them.
Trastuzumab; Hyaluronidase: (Minor) H1-blockers (antihistamines), when given in large systemic doses, may render tissues partially resistant to the action of hyaluronidase. Patients receiving these medications may require larger amounts of hyaluronidase for equivalent dispersing effect.

Trazodone: (Moderate) Antihistamines that may cause sedation, such as chlorpheniramine, should be used cautiously in patients receiving trazodone because of additive CNS-depressant effects.
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.
Triamcinolone: (Moderate) The therapeutic effect of phenylephrine may be increased in patient receiving corticosteroids, such as hydrocortisone. Monitor patients for increased pressor effect if these agents are administered concomitantly.
Triamterene: (Moderate) The cardiovascular effects of sympathomimetics may reduce the antihypertensive effects produced by diuretics. Well-controlled hypertensive patients receiving decongestant sympathomimetics at recommended doses do not appear at high risk for significant elevations in blood pressure, however, increased blood pressure has been reported in some patients.
Triazolam: (Moderate) The therapeutic effect of phenylephrine may be decreased in patients receiving benzodiazepines. Monitor patients for decreased pressor effect if these agents are administered concomitantly.
Tricyclic antidepressants: (Major) Tricyclic antidepressants (TCAs) may markedly enhance the pressor response to parenteral direct-acting sympathomimetic agents such as norepinephrine and, to a lesser extent, epinephrine and phenylephrine. TCAs inhibit norepinephrine reuptake in adrenergic neurons, resulting in increased stimulation of adrenergic receptors. Clinically, the patient might experience hypertension, headache, tremor, palpitations, chest pain, or irregular heartbeat. (Moderate) Additive anticholinergic and CNS effects may be seen when tricyclic antidepressants are used concomitantly with sedating H1-blockers. Antimuscarinic effects might be seen not only on GI smooth muscle, but also on bladder function, the eye, and temperature regulation.
Trifluoperazine: (Moderate) Additive anticholinergic and sedative effects may be seen when trifluoperazine is used with first generation antihistamines, such as chlorpheniramine. Patients should be informed to read non-prescription cough and cold product labels carefully for additional interacting antihistamines.
Trimethobenzamide: (Moderate) The concurrent use of trimethobenzamide with other medications that cause CNS depression, like the sedating h1-blockers, may potentiate the effects of either trimethobenzamide or the sedating h1-blocker.
Trospium: (Moderate) Additive anticholinergic effects may be seen when trospium is used concomitantly with drugs that are known to possess relatively significant antimuscarinic properties, including sedating H1-blockers. Clinicians should note that additive antimuscarinic effects may be seen not only on GI smooth muscle, but also on bladder function and temperature regulation. While CNS-related side effects such as drowsiness and blurred vision are not typically noted with trospium, they may occur in some patients.
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.
Vardenafil: (Minor) The therapeutic effect of phenylephrine injection may be decreased in patients receiving phosphodiesterase inhibitors. A decreased pressor effect of phenylephrine might occur. Monitor

for proper blood pressure when these drugs are used together,

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.

Vemurafenib: (Moderate) Concomitant use of vemurafenib and chlorpheniramine may result in increased chlorpheniramine concentrations. Chlorpheniramine is metabolized by CYP2D6 and vemurafenib is a weak CYP2D6 inhibitor. Monitor patients for toxicity.

Verapamil: (Moderate) Phenylephrine's cardiovascular effects may reduce the antihypertensive effects of calcium-channel blockers. Well-controlled hypertensive patients receiving decongestant sympathomimetics at recommended doses do not appear to be at high risk for significant elevations in blood pressure; however, increased blood pressure (especially systolic hypertension) has been reported in some patients.

Vigabatrin: (Moderate) Vigabatrin may cause somnolence and fatigue. Drugs that can cause CNS depression, if used concomitantly with vigabatrin, may increase both the frequency and the intensity of adverse effects such as drowsiness, sedation, and dizziness. Caution should be used when vigabatrin is given with sedating H1-blockers.

Vilazodone: (Moderate) Due to the CNS effects of vilazodone, caution should be used when vilazodone is given in combination with other centrally acting medications such as anxiolytics, sedatives, and hypnotics. Also, Cyproheptadine is an antagonist of serotonin in the CNS, a property which may oppose some of the pharmacologic effects of vilazodone. Cyproheptadine has been used for the management of orgasm dysfunction caused by the serotonergic antidepressants and for the adjunctive treatment of serotonin syndrome; however, a reversal of antidepressant effects may occur when cyproheptadine is given in a routine manner along with the antidepressant. Clinically, cyproheptadine reportedly has interfered with the antidepressant and anti-bulimia actions of fluoxetine, but more data are needed to confirm a direct drug-drug interaction.

Yohimbine: (Major) At high doses, yohimbine may nonselectively inhibit MAO and also, at normal doses, activates the sympathetic nervous system. Traditional MAOIs can cause serious adverse effects when taken concomitantly with sympathomimetics.

Zaleplon: (Moderate) In premarketing studies, zaleplon potentiated the CNS effects of ethanol, imipramine, and thioridazine for at least 2 to 4 hours. Other drugs that may have additive CNS effects with zaleplon but have not been studied include other sedating H1-blockers. If used together, a reduction in the dose of one or both drugs may be needed.

Ziconotide: (Moderate) Sedating H1-blockers are CNS depressant medications that may increase drowsiness, dizziness, and confusion that are associated with ziconotide.

Ziprasidone: (Moderate) Sedating H1-blockers are associated with sedation; therefore, additive effects may be seen during concurrent use with other drugs having CNS depressant properties such as antipsychotics. Additive drowsiness or other CNS effects may occur with ziprasidone.

Zolpidem: (Moderate) The CNS-depressant effects of zolpidem can be potentiated with concomitant administration of other drugs known to cause CNS depression, such as sedating H1-blockers. A dose reduction of either or both drugs should be considered to minimize additive sedative effects. For Intermezzo brand of sublingual zolpidem tablets, reduce the dose to 1.75 mg/night. The risk of next-day psychomotor impairment is increased during co-administration, which may decrease the ability to perform tasks requiring full mental alertness such as driving. In addition, sleep-related behaviors, such as sleep-

driving, are more likely to occur during concurrent use of zolpidem and other CNS depressants than with zolpidem alone.

PREGNANCY AND LACTATION

Pregnancy

Chlorpheniramine; phenylephrine is contraindicated during breast-feeding. The effects of chlorpheniramine or phenylephrine in nursing infants is unknown but may manifest as irritability, disturbed sleeping patterns, drowsiness, hyperexcitability, or excessive crying. Alternative methods of feeding should be used if routine therapy is necessary in the breast-feeding mother.

5.1 MECHANISM OF ACTION

This antihistamine-decongestant combination acts synergistically for relief of upper respiratory symptoms such as nasal congestion, rhinorrhea, and sneezing associated with allergic rhinitis, vasomotor rhinitis, the common cold, or sinusitis.

•Chlorpheniramine: H1-antagonists do not prevent the release of histamine, as do cromolyn and nedocromil, but rather compete with free histamine for binding at H1-receptor sites. These drugs competitively antagonize the effects of histamine on H1-receptors in the GI tract, uterus, large blood vessels, and bronchial smooth muscle. Blockade of H1-receptors also suppresses the formation of edema, flare, and pruritus that result from histaminic activity. H1-antagonists also possess anticholinergic properties in varying degrees. The anticholinergic activity of propylamine derivatives such as chlorpheniramine is moderate. This anticholinergic action appears to be due to a central antimuscarinic effect. Sedative effects from chlorpheniramine result from antagonism at central histaminergic receptors. Chronic administration may lead to some degree of tolerance.

•Phenylephrine: Phenylephrine possesses both direct and indirect sympathomimetic effects, primarily as a postsynaptic alpha-adrenergic agonist, producing potent vasoconstriction. An indirect effect due to the release of norepinephrine plays a small role in the overall action of phenylephrine. Phenylephrine does not stimulate beta2-adrenergic receptors in the bronchi or peripheral blood vessels or beta1-adrenergic receptors of the heart. Phenylephrine increases resistance and, to a lesser extent, decreases capacitance of blood vessels. Following oral administration, constriction of blood vessels leads to reduced blood flow to the nose, decreased amount of blood in the sinusoid vessels, and decreased mucosal edema, which relieves nasal congestion.

PHARMACOKINETICS

Chlorpheniramine; phenylephrine combinations are administered orally. Pharmacokinetic data for combination products is unavailable, although data obtained from single agent use is likely applicable to many combination formulations.

Chlorpheniramine: Chlorpheniramine is widely distributed in body tissues and fluids, and it crosses the placenta and is excreted into breast milk. Metabolism of chlorpheniramine is extensive and rapid, first occurring in the gastric mucosa and then on first-pass through the liver, which may be saturable. N-dealkylation produces several metabolites, which are excreted in the urine along with the parent compound. Plasma half-life is between 2—4 hours, but the terminal elimination half-life varies with age. The half-life in healthy adults is 20—24 hours. Excretion rates are dependent on the pH of urine and urinary flow, with the rate decreasing as the pH rises and urinary flow decreases.

Phenylephrine: Phenylephrine is metabolized in the liver and intestine by monoamine oxidase. The metabolites and their route and rate of excretion have not been fully identified. The pharmacologic effect of phenylephrine is terminated at least in part by uptake of the drug into tissues.

Oral Route

Chlorpheniramine: Chlorpheniramine is well absorbed from the GI tract. Food delays absorption; however, bioavailability is not affected. Onset of action of chlorpheniramine when used as a single agent in regular-release formulations is about 30—60 minutes, with Cmax occurring in about 2 hours and maximum therapeutic effect in about 6 hours. The duration of action is between 4—8 hours. Protein binding is approximately 72%. Metabolism of chlorpheniramine is extensive and rapid, first occurring in the gastric mucosa and then on first-pass through the liver, which may be saturable.

Phenylephrine: Phenylephrine is irregularly absorbed from and readily metabolized in the GI tract. The bioavailability of phenylephrine is about 38%. Following oral administration of phenylephrine as a single agent, nasal decongestion occurs within 15—20 minutes and persists for up to 4 hours.

6.5 Nature and contents of container

Pack sizes: Blister Of 10 Capsules.

SOLE AGENT :.Nkoyo Chemists

NAFDAC REG. NO. : 04-8784

For the use of Registered medical Practitioner or a Hospital or a Laboratory only.

COLMAN CAPSULES

(Chlorpheniramine Maleate & Phenylephrine Hydrochloride Capsules)

COMPOSITION

Each capsule contains :
Chlorpheniramine Maleate BP.....4 mg
Phenylephrine Hydrochloride BP.....2.5 mg

INDICATIONS

COLMAN CAPSULES is indicated in the treatment of temporarily relieves nasal congestion due to the common cold, hay fever or other upper respiratory allergies and associated with sinusitis. Temporarily relieves runny nose and reduces sneezing, itching of the nose or throat and itchy, watery eyes due to hay fever or other upper respiratory allergies. Helps clear nasal passages; shrinks swollen membranes. Helps decongest sinus openings and passages; temporarily relieves sinus congestion and pressure.

CONTRAINDICATIONS

COLMANCAPSULES is contraindicated in patients receiving MAO inhibitors, in patients with a known hypersensitivity to any of the ingredients, and in patients with glaucoma, hypertension, cardiac disease, or hyperthyroidism.

DOSAGE

Adults and children 12 years of age and older: 1 or 2 Capsules every 4 hours. Children 6 to under 12 years of age : 1 capsules every 4 hours. Do not exceed 4 doses in 24 hours.

PRECAUTIONS

General: Usecautiously, if at all, in the presence of pyloric obstruction. Use with caution in those over 40 years of age, in the presence of diabetes mellitus or urinary retention, and in men with prostatic hypertrophy or a history of bladder difficulty. If disturbances in urination occur, medication should be discontinued for 1 or 2 days and then resumed at a lower dosage. Antihistamines may cause excitability, especially in children. Information for patients : Becausethis product may cause blurring of vision or drowsiness, patients should be cautioned against driving or operating machinery.

DRUG INTERACTIONS

MAO inhibitors and beta adrenergic blockers increase the effects of sympathomimetics. Sympathomimetics may reduce the antihypertensive effects of methyldopa, guanethidine, mecamylamine, reserpine and veratrum alkaloids. Concomitant use of antihistamines with alcohol or other CNS depressants may have an additive effect. Pregnancy : Pregnancy Category C. It is also not known whether the product can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. The product should be given to a pregnant woman only if clearly needed. Nursing mothers : It is not known whether these drugs are excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when this product is administered to a nursing woman. Pediatric use : Safety and effectiveness in children below the age of 6 have not been established.

Geriatric use : Anticholinergic and CNS stimulant effects more likely to occur in older patients; danger of precipitating undiagnosed glaucoma, possible impairment of memory.

ADVERSE REACTIONS

Side effects include xerostomia, blurred vision, bradycardia, mydriasis, flushing, palpitation, dizziness, constipation, urinary retention, drowsiness, increased irritability or excitability, nause a or dysphagia.

OVERDOSAGE

The Stomach should be emptied promptly by lavage or by induction of emesis (syrup of ipecac recommended). The installation of activated charcoal into the stomach also should be considered. If respiratory depression is present, treat promptly with oxygen and/or mechanical support of ventilation. If convulsions or marked CNS excitement occurs, only short-acting benzodiazepine-type drugs should be used.

STORAGE CONDITIONS

Store in a cool place and protect from light.
Keep all medicines out of reach of children.

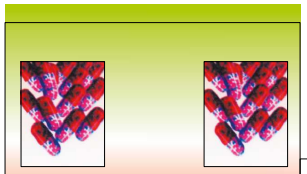
PRESENTATION

Blister pack of 10 capsules.

Mfg. Lic No.: KD-493
Nafdac Reg. No.: 04-8784

Manufactured By :
Mancare
PHARMACEUTICALS PVT. LTD.
Plot No. 59, 60, 85, 86, V.M.I.E, Dowali Village, Vasai (W), Dist. Thane, Maharashtra, India.
E-mail: mancerp@yahoo.co.in

Sole Agent:
Nkoyo Chemists
18, Ukpor Street, Fegge, Onitsha,
Anambra State, Nigeria.



NAFDAC REG. NO.: 04-8784

COLMAN

10 x 10 capsules

83 X 77 X 62mm
10June2014

10 x 10 capsules

COLMAN

NAFDAC REG. NO.: 04-8784

Composition:
Each capsule contains :
Chlorpheniramine Maleate B.P. .....4 mg.
Phenylephrine Hydrochloride B.P. .....2.5 mg.

Empty heard gelatin capsule shell
contains approved colours
Store in a cool, dry & dark place.

Keep all medicines out of reach of children.

Dosage: As directed by the Physician.

Sole Agent:
Nkoyo Chemists
18, Ukpor Street Fegge, Onitsha,
Anambra State, Nigeria.

10 x 10 capsules

COLMAN

NAFDAC REG. NO.: 04-8784

Caution: **COLMAN** may cause drowsiness in some patients. Driving of vehicles & running of machinery is contra-indicated during therapy.

Mfg. Lic. No. : KD-493
Batch No. :
Mfg Date :
Exp Date :

Manufactured By :
Mancare
PHARMACEUTICALS PVT. LTD.
Plot No. 59, 60, 85, 86, V.M.I.E, Dowali Village,
Vasai (W), Dist. Thane, Maharashtra, India.
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