Name of the medicinal product :

DECNESE

Qualitative and quantitative composition :

Each uncoated tablet contains:-

Chlorpropamide B.P..250mg

Pharmaceuticals form : Tablets

White, circular, flat , uncoated tablets flat round punches embossed ""DIA & 250" with Break Line on one side and plain on one other side

DOSAGE & INDICATIONS

For the treatment of type 2 diabetes mellitus as an adjunct to diet and exercise.

Oral dosage

Adults

Initially, 250 mg PO once daily with breakfast or in divided doses if GI intolerance occurs. Increase dosage by 50 to 125 mg every 3 to 5 days if needed to attain glycemic goals. Usual dosing: Most moderately severe, stable type 2 DM patients are controlled by 250 mg/day PO. Some less severe type 2 DM patients may do well on 100 mg/day or less. Patient with more severe disease may require 500 mg/day for adequate control. Patients who fail to respond to a maintenance dose of 500 mg/day do not generally respond to higher doses. Max: 750 mg/day PO. SWITCHING FROM OTHER MEDICATIONS: No transition period is necessary when transferring patients from other oral hypoglycemic agents to chlorpropamide. Some type 2 DM patients treated with insulin can be switched successfully to chlorpropamide therapy. Patients receiving 40 units/day or less of insulin can be placed directly on chlorpropamide and insulin can be abruptly discontinued. Patients requiring more than 40 units/day of insulin should receive chlorpropamide along with a 50% reduction in insulin dose. May further decrease insulin based on the response. During insulin reduction and discontinuation, patients should test blood glucose frequently and contact the prescriber if blood glucose is outside the acceptable range.

Geriatric Adults

Avoid use in elderly patients due to the risk of prolonged hypoglycemia and prolonged half-life in older adults. If this drug is necessary, use a reduced initial dose of 100 to 125 mg PO once daily, followed by careful dosage titration to achieve clinical goals.

For the treatment of central diabetes insipidus†.

Oral dosage

Adults

125 to 250 mg PO once daily. Due to the risk of hypoglycemia, chlorpropamide is considered to be an alternative to standardly accepted and indicated treatments (e.g., DDAVP). The drug is ineffective in treating nephrogenic diabetes insipidus.

†Indicates off-label use

MAXIMUM DOSAGE

Adults

750 mg/day PO.

Elderly

Avoid use.

Adolescents

Safety and efficacy have not been established.

Children

Safety and efficacy have not been established.

Infants

Safety and efficacy have not been established.

Neonates

Safety and efficacy have not been established.

DOSING CONSIDERATIONS

Hepatic Impairment

Lower doses are recommended in patients with hepatic impairment, since chlorpropamide is extensively metabolized by the liver.

Renal Impairment

CrCl more than 80 mL/minute: No dosage adjustment needed.
CrCl 51 to 80 mL/minute: Reduce dosage by 50%.
CrCl 50 mL/minute or less: Avoid use.

ADMINISTRATION

NOTE: Oral hypoglycemic dosages should be individualized. Periodic monitoring of blood glucose is necessary to determine the lowest effective dose.

NOTE: The normal starting dose of chlorpropamide may be used when transferring patients from other sulfonylureas. The discontinued drug may be stopped abruptly, and chlorpropamide started at once.

Oral Administration

Administer in the morning with breakfast.
Occasionally, gastrointestinal intolerance can be reduced by dividing the dose.

STORAGE

DECNESE:
- Protect from light
- Store at controlled room temperature (between 68 and 77 degrees F)

CONTRAINDICATIONS / PRECAUTIONS

General Information

There are conflicting studies regarding the possible cardiovascular risks associated with the use of oral sulfonylurea antidiabetic agents (e.g., chlorpropamide). The largest of the trials, the United Kingdom Prospective Diabetes Study (UKPDS), has demonstrated that intensive therapy with sulfonylureas does not increase the risk of myocardial infarction or diabetes-related death when compared to conventional therapy. In this trial, lowering blood glucose with sulfonylurea therapy did not significantly effect cardiovascular complications. A 16% reduction (not statistically significant) in the risk of combined fatal or nonfatal myocardial infarction and sudden death has been reported. In a follow-up study to the UKPDS, researchers found that after 10-years of resuming typical care, patients originally randomized to intensive therapy with sulfonylureas or insulin had a 15% relative reduction (RR 0.85, 95% CI 0.74—0.97; p=0.01) in the risk of myocardial infarction and a 13% relative decrease (RR 0.87, 95% CI 0.76—0.96; p=0.007) in the risk of death from any cause as compared to patients originally randomized to conventional therapy; it should be noted that these reductions in cardiovascular risks persisted even though HbA1c concentrations were similar in the 2 groups after 1 year of follow-up. In contrast, the University Group Diabetes Program (UGDP) has previously reported that the administration of oral sulfonylureas increases cardiovascular mortality compared with dietary management alone, or dietary management and insulin therapy. The UGDP study has been widely criticized for study limitations including a small sample size (i.e., 200 patients per treatment group). Despite the controversy regarding these findings, the results of the UGDP study serve as a basis for the manufacturers' warning of possible risk of cardiovascular mortality associated with the use of oral sulfonylureas.

Sulfonylurea hypersensitivity

Chlorpropamide is contraindicated in patients with a known chlorpropamide hypersensitivity; it should be used with caution in patients with sulfonylurea hypersensitivity.

Sulfonamide hypersensitivity

It may be prudent to monitor patients with a known history of sulfonamide hypersensitivity for allergic-type reactions when initiating chlorpropamide. Although they contain a sulfonamide side chain, sulfonylureas and other nonantibiotic sulfonamides do not contain the N4 aromatic amine or the N1-substituent that are present in sulfonamide antibiotics and thought to be responsible for hypersensitivity-type adverse reactions; the risk of cross-sensitivity in patients taking a nonantibiotic sulfonamide that have

a history of sulfonamide hypersensitivity is low and has been confirmed by recent, observational studies. However, several cases in the literature report of cross-sensitivity reactions to sulfonylureas in patients with a history of sulfonamide hypersensitivity. A 57 year-old man with a self-reported sulfonamide allergy (unknown offending agent) and stable on hydrochlorothiazide and glyburide experienced possible erythema multiforme, an acute inflammatory skin reaction, and throat swelling within 30 days after initiating celecoxib, which contains a sulfonamide side chain. Although the skin reaction resolved with celecoxib discontinuation, a similar reaction occurred when glyburide and hydrochlorothiazide therapies were re-introduced. In another case report, a 71 year-old man with multiple, documented drug allergies including Stevens-Johnson syndrome to trimethoprim-sulfamethoxazole experienced a rash after receiving furosemide and after receiving glyburide, both of which contain a sulfonamide side chain. It should be noted that this patient also had a history of several non-sulfonamide allergies; he subsequently received torsemide, which also contains a sulfonamide side chain, without problems. In general, patients with a history of hypersensitivity to any drug are predisposed for subsequent hypersensitivity reactions to other drugs. Because of this, patients with a history of sulfonamide hypersensitivity should be monitored for hypersensitivity reactions to other drugs, including sulfonylureas; however, treatment with a nonantibiotic sulfonamide may not need to be withheld in patients with a sulfonamide allergy as long as patients are monitored appropriately, especially if alternative therapies are not available.

Fever, infection, surgery, trauma

Temporary use of insulin may be necessary during periods of physiologic stress (e.g., systemic infection, trauma, surgery, or fever) in patients receiving oral antidiabetic agents (e.g., chlorpropamide). Stress can induce alterations in glucose regulation that can be controlled only with exogenously administered insulin.

Diabetic ketoacidosis, type 1 diabetes mellitus

Chlorpropamide is contraindicated in patients with type 1 diabetes mellitus or diabetic ketoacidosis, with or without coma.

Thyroid disease

Thyroid hormone increases the gastrointestinal absorption of glucose, as well as stimulates gluconeogenesis and glycogenolysis. Patients with both thyroid disease and diabetes mellitus (and receiving chlorpropamide therapy) must be treated for both diseases.

Ascites, heart failure, hepatic disease, hypoglycemia, porphyria, renal disease, renal failure, renal impairment

Chlorpropamide should be avoided in patients with renal disease associated with moderate to severe renal impairment (CrCl less than 50 mL/min) or renal failure. Chlorpropamide should be used with caution in patients with hepatic disease. Renal impairment or hepatic disease can cause elevations in chlorpropamide drug concentrations and hepatic disease can reduce gluconeogenic capacity; both problems increase the risk of hypoglycemia. In addition, the potential antidiuretic properties of chlorpropamide could worsen edema associated with hepatic cirrhosis (e.g., ascites) or heart failure. Chlorpropamide, like other sulfonylurea agents, can exacerbate hepatic porphyria and should be used cautiously in patients with a history of this condition.

Neonates, obstetric delivery, pregnancy

Chlorpropamide should be given during pregnancy only if the potential benefits justify the potential risk to the patient and fetus. Animal reproduction studies have not been conducted with chlorpropamide. One surveillance study of 18 newborns who were exposed to chlorpropamide during the 1st trimester revealed no major defects, and another study found that 6 infants who were exposed in utero to chlorpropamide during the first trimester experienced congenital defects. Sulfonylureas are not likely to provide good glucose control in pregnant women who cannot be controlled on diet alone. Prolonged severe hypoglycemia (4 to 10 days) has been reported in neonates born to mothers who were receiving a sulfonylurea drug at the time of obstetric delivery. This has been reported more frequently with the use of agents with prolonged half-lives. If chlorpropamide is used during pregnancy, it should be discontinued at least 1 month before the expected delivery date and other therapies instituted to maintain blood glucose levels as close to normal as possible. Chlorpropamide, when administered near term, crosses the placenta and may persist in the neonatal serum for 4 to 6 days, due to the long half-life. Several case reports or neonatal hypoglycemia are described in the literature, while one study showed no evidence for neonatal hypoglycemia at maternal doses of 100 to 200 mg/day or more. The American College of Obstetricians and Gynecologists (ACOG) and the American Diabetes Association (ADA) continue to recommend human insulin as the standard of care in women with diabetes mellitus and gestational diabetes mellitus (GDM) requiring medical therapy; insulin does not cross the placenta.

Breast-feeding

Chlorpropamide is excreted into breast milk. Because of the possibility of hypoglycemia or other effects in nursing infants, it is recommended that chlorpropamide not be used in women who are breast-feeding. One report describes a woman who received chlorpropamide 500 mg and had an analysis of two samples of breast milk performed 5 hours post-dose; chlorpropamide concentration was 5 mcg/ml (normal peak blood level after a single 250 mg dose = 30 mcg/ml). Other oral hypoglycemics may be considered as possible alternatives during breast-feeding. Because acarbose has limited systemic absorption, which results in minimal maternal plasma concentrations, clinically significant exposure via breast milk is not expected. Also, while the manufacturers of metformin recommend against breast-feeding while taking the drug, data have shown that metformin is excreted into breast milk in small amounts and adverse effects on infant plasma glucose have not been reported in human studies. The American Academy of Pediatrics (AAP) regards tolbutamide as usually compatible with breast-feeding. Although other sulfonylureas have not been evaluated by the AAP, although, glyburide may be a suitable alternative since it was not detected in the breast milk of lactating women who received single and multiple doses of glyburide. If any oral hypoglycemics are used during breast feeding, the nursing infant should be monitored for signs of hypoglycemia, such as increased fussiness or somnolence.

Children

Safe and effective use of chlorpropamide has not been established in children. Experience with the use of oral hypoglycemics is limited in children, who rarely are affected by type-2 diabetes. Chlorpropamide is not effective in treating juvenile onset type-1diabetics, who are insulin-dependent.

G6PD deficiency

Patients with glucose-6-phosphate dehydrogenase deficiency (G6PD deficiency) who take chlorpropamide may be at risk for hemolytic anemia; consider using a non-sulfonylurea alternative in these patients.

Geriatric

According to the Beers Criteria, chlorpropamide is considered a potentially inappropriate medication (PIM) in geriatric patients with diabetes and should be avoided. Chlorpropamide has a prolonged half-life in older adults and has been associated with severe and prolonged hypoglycemia and may cause the syndrome of inappropriate antidiuretic hormone secretion (SIADH). The federal Omnibus Budget Reconciliation Act (OBRA) regulates medication use in residents of long-term care facilities (LTCFs). According to OBRA, the use of antidiabetic medications should include monitoring (e.g., periodic blood glucose) for effectiveness based on desired goals for that individual and to identify complications of treatment such as hypoglycemia or impaired renal function. Chlorpropamide is not considered a hypoglycemic agent of choice in older adults because of the long half-life and/or duration of action and its increased risk of prolonged and serious hypoglycemia, with symptoms including tachycardia, palpitations, irritability, headache, hypothermia, visual disturbances, lethargy, confusion, seizures, and/or coma. Sulfonylureas such as chlorpropamide can cause SIADH and result in hyponatremia.

ADVERSE REACTIONS

Severe

erythema multiforme / Delayed / 0-1.0
exfoliative dermatitis / Delayed / 0-1.0
hepatic failure / Delayed / 0-0.1
angioedema / Rapid / 0-0.1
vasculitis / Delayed / 0-0.1
agranulocytosis / Delayed / 0-0.1
aplastic anemia / Delayed / 0-0.1
hemolytic anemia / Delayed / 0-0.1
pancytopenia / Delayed / 0-0.1
SIADH / Delayed / 0-0.1
secondary failure / Delayed / 10.0
porphyria / Delayed / Incidence not known

Moderate

hypoglycemia / Early / 1.8-39.0
hepatitis / Delayed / 0-1.0
elevated hepatic enzymes / Delayed / 0-1.0
cholestasis / Delayed / 0-1.0
jaundice / Delayed / 0-1.0
thrombocytopenia / Delayed / 0-0.1
leukopenia / Delayed / 0-0.1
eosinophilia / Delayed / 0-0.1
hemolysis / Early / 0-0.1
hyponatremia / Delayed / 0-0.1
blurred vision / Early / Incidence not known

Mild

nausea / Early / 0-5.0
pruritus / Rapid / 0-3.0
diarrhea / Early / 0-2.0

anorexia / Delayed / 0-2.0
vomiting / Early / 0-2.0
maculopapular rash / Early / 0-1.0
urticaria / Rapid / 0-1.0
arthralgia / Delayed / 0-0.1
myalgia / Early / 0-0.1
flushing / Rapid / 0-0.1
weight gain / Delayed / 10.0
headache / Early / Incidence not known
dizziness / Early / Incidence not known
photosensitivity / Delayed / Incidence not known

DRUG INTERACTIONS

Acebutolol: (Moderate) Increased frequency of blood glucose monitoring may be required when a beta blocker is given with antidiabetic agents. Since beta blockers inhibit the release of catecholamines, these medications may hide symptoms of hypoglycemia such as tremor, tachycardia, and blood pressure changes. Other symptoms, like headache, dizziness, nervousness, mood changes, or hunger are not blunted. Beta-blockers also exert complex actions on the body's ability to regulate blood glucose. Some beta-blockers, particularly non-selective beta-blockers such as propranolol, have been noted to potentiate insulin-induced hypoglycemia and a delay in recovery of blood glucose to normal levels. Hyperglycemia has been reported as well and is possibly due to beta-2 receptor blockade in the beta cells of the pancreas. A selective beta-blocker may be preferred in patients with diabetes mellitus, if appropriate for the patient's condition. Selective beta-blockers, such as atenolol or metoprolol, do not appear to potentiate insulin-induced hypoglycemia. While beta-blockers may have negative effects on glycemic control, they reduce the risk of cardiovascular disease and stroke in patients with diabetes and their use should not be avoided in patients with compelling indications for beta-blocker therapy when no other contraindications are present.
Acetaminophen; Aspirin, ASA; Caffeine: (Moderate) Monitor blood glucose during concomitant sulfonylurea and aspirin use. Concomitant use may cause an increased blood glucose-lowering effect with risk of hypoglycemia.
Acetaminophen; Aspirin: (Moderate) Monitor blood glucose during concomitant sulfonylurea and aspirin use. Concomitant use may cause an increased blood glucose-lowering effect with risk of hypoglycemia.
Acetaminophen; Aspirin; Diphenhydramine: (Moderate) Monitor blood glucose during concomitant sulfonylurea and aspirin use. Concomitant use may cause an increased blood glucose-lowering effect with risk of hypoglycemia.
Acetaminophen; Caffeine; Magnesium Salicylate; Phenyltoloxamine: (Moderate) If salicylates and sulfonylureas are to be administered together, patients should be monitored for changes in glycemic control. Salicylates, by inhibiting prostaglandin E2 synthesis, can indirectly increase insulin secretion. Thus, salicylates can decrease blood sugar and may potentiate the effects of other antidiabetic agents. This mechanism may explain how salicylates can potentiate the clinical effects of sulfonylureas; however, displacement of sulfonylureas from protein binding sites has also been reported. In large doses, salicylates uncouple oxidative phosphorylation, deplete hepatic and muscle glycogen, and cause hyperglycemia and glycosuria.
Acetaminophen; Chlorpheniramine; Dextromethorphan; Phenylephrine: (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.

Acetaminophen; Chlorpheniramine; Dextromethorphan; Pseudoephedrine: (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.

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Acetaminophen; Dextromethorphan; Guaifenesin; Phenylephrine: (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.

Acetaminophen; Dextromethorphan; Guaifenesin; Pseudoephedrine: (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.

Acetaminophen; Dextromethorphan; Phenylephrine: (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.

Acetaminophen; Dextromethorphan; Pseudoephedrine: (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.

Acetaminophen; Dichloralphenazone; Isometheptene: (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.

Acetaminophen; Guaifenesin; Phenylephrine: (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.

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Acitretin: (Moderate) Retinoids have been reported to cause changes in blood sugar control in diabetics. In a study of 7 healthy male volunteers, acitretin treatment potentiated the blood glucose lowering effect of glibenclamide (a sulfonylurea similar to chlorpropamide) in 3 of the 7 subjects. Repeating the study with 6 healthy male volunteers in the absence of glibenclamide did not detect an effect of acitretin on glucose tolerance. Careful supervision of diabetic patients under treatment with acitretin is recommended, especially those taking concomitant sulfonylureas. There appears to be no pharmacokinetic interaction between acitretin and glyburide.

Acrivastine; Pseudoephedrine: (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.
Aliskiren; Valsartan: (Moderate) Monitor blood glucose during concomitant sulfonylurea and angiotensin receptor blocker use. Concomitant use may cause an increased blood glucose-lowering effect with risk of hypoglycemia.
Alkalinizing Agents: (Moderate) Urinary alkalinizing agents may increase the excretion of chlorpropamide by increasing renal clearance. Monitor for decreased efficacy of chlorpropamide (i.e., increased blood glucose) during coadministration.
Allopurinol: (Minor) Limited evidence suggests that concurrent allopurinol can interfere with chlorpropamide elimination. It is proposed that allopurinol interferes with renal tubular secretion of chlorpropamide. If allopurinol is added to chlorpropamide therapy, patients should be monitored for hypoglycemia.
Alogliptin; Metformin: (Moderate) Monitor blood glucose during concomitant sulfonylurea and metformin use; a sulfonylurea dose adjustment may be necessary. Concomitant use may cause an increased blood glucose-lowering effect with risk of hypoglycemia.
Alogliptin; Pioglitazone: (Moderate) If hypoglycemia occurs during concomitant use of pioglitazone and a sulfonylurea, reduce the dose of the sulfonylurea. Patients receiving pioglitazone in combination with sulfonylureas may be at risk for hypoglycemia.
Aminolevulinic Acid: (Moderate) Additive photosensitization may be seen with concurrent administration of sulfonylureas and other photosensitizing agents. Prevention of photosensitivity includes adequate protection from sources of UV radiation (e.g., avoiding sun exposure and tanning booths) and the use of protective clothing and sunscreens on exposed skin
Amiodarone: (Minor) Amiodarone inhibits cytochrome P450 2C9. Caution is recommended when administering amiodarone with other CYP2C9 substrates including sulfonylureas.
Amlodipine; Benazepril: (Moderate) Monitor blood glucose during concomitant sulfonylurea and angiotensin-converting enzyme (ACE) inhibitor use. Concomitant use may cause an increased blood glucose-lowering effect with risk of hypoglycemia.
Amlodipine; Olmesartan: (Moderate) Monitor blood glucose during concomitant sulfonylurea and angiotensin receptor blocker use. Concomitant use may cause an increased blood glucose-lowering effect with risk of hypoglycemia.
Amlodipine; Valsartan: (Moderate) Monitor blood glucose during concomitant sulfonylurea and angiotensin receptor blocker use. Concomitant use may cause an increased blood glucose-lowering effect with risk of hypoglycemia.
Amlodipine; Valsartan; Hydrochlorothiazide, HCTZ: (Moderate) Monitor blood glucose during concomitant sulfonylurea and angiotensin receptor blocker use. Concomitant use may cause an increased blood glucose-lowering effect with risk of hypoglycemia.
Ammonium Chloride: (Minor) Ammonium chloride decreases the clearance of chlorpropamide by acidifying the urine. Plasma concentrations of chlorpropamide can increase, which can cause hypoglycemia.
Amoxicillin; Clarithromycin; Omeprazole: (Moderate) The concomitant use of clarithromycin and antidiabetic agents can result in significant hypoglycemia. Careful monitoring of blood glucose is recommended.
Amphetamine: (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.
Amphetamine; Dextroamphetamine: (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.
Amprenavir: (Moderate) New onset diabetes mellitus, exacerbation of diabetes mellitus, and hyperglycemia due to insulin resistance have been reported with use of anti-retroviral protease inhibitors. A possible mechanism is impairment of beta-cell function. Onset averaged approximately 63 days after initiating protease inhibitor therapy, but has occurred as early as 4 days after beginning therapy. Diabetic ketoacidosis has occurred in some patients including patients who were not diabetic prior to protease inhibitor treatment. Patients on antidiabetic agents should be closely monitored for changes in glycemic control, specifically hyperglycemia, if protease inhibitor therapy is initiated.
Androgens: (Moderate) Changes in insulin sensitivity or glycemic control may occur in patients treated with androgens. In diabetic patients, the metabolic effects of androgens may decrease blood glucose and, therefore, may decrease antidiabetic agent dosage requirements. Monitor blood glucose and HbA1C when these drugs are used together.
Angiotensin II receptor antagonists: (Moderate) Monitor blood glucose during concomitant sulfonylurea and angiotensin receptor blocker use. Concomitant use may cause an increased blood glucose-lowering effect with risk of hypoglycemia.
Angiotensin-converting enzyme inhibitors: (Moderate) Monitor blood glucose during concomitant sulfonylurea and angiotensin-converting enzyme (ACE) inhibitor use. Concomitant use may cause an increased blood glucose-lowering effect with risk of hypoglycemia.
Aprepitant, Fosaprepitant: (Minor) Use caution if chlorpropamide and aprepitant are used concurrently and monitor for a possible decrease in the efficacy of chlorpropamide. After administration, fosaprepitant is rapidly converted to aprepitant and shares the same drug interactions. Chlorpropamide is a CYP2C9 substrate and aprepitant is a CYP2C9 inducer. Administration of a CYP2C9 substrate, tolbutamide, on days 1, 4, 8, and 15 with a 3-day regimen of oral aprepitant (125 mg/80 mg/80 mg) decreased the tolbutamide AUC by 23% on day 4, 28% on day 8, and 15% on day 15. The AUC of tolbutamide was decreased by 8% on day 2, 16% on day 4, 15% on day 8, and 10% on day 15 when given prior to oral administration of aprepitant 40 mg on day 1, and on days 2, 4, 8, and 15. The effects of aprepitant on tolbutamide were not considered significant. When a 3-day regimen of aprepitant (125 mg/80 mg/80 mg) given to healthy patients on stabilized chronic warfarin therapy (another CYP2C9 substrate), a 34% decrease in S-warfarin trough concentrations was noted, accompanied by a 14% decrease in the INR at five days after completion of aprepitant.
Aripiprazole: (Moderate) Atypical antipsychotic therapy may aggravate diabetes mellitus and cause metabolic changes such as hyperglycemia. Monitor patients on antidiabetic agents for worsening glycemic control. The atypical antipsychotics have been associated with metabolic changes, including hyperglycemia, diabetic ketoacidosis, hyperosmolar, hyperglycemic states, and diabetic coma. Aggravation of diabetes mellitus has been reported. Possible mechanisms include atypical antipsychotic-

induced insulin resistance or direct beta-cell inhibition.
Articaine; Epinephrine: (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.
Asenapine: (Moderate) Atypical antipsychotic therapy may aggravate diabetes mellitus and cause metabolic changes such as hyperglycemia. Monitor patients on antidiabetic agents for worsening glycemic control. The atypical antipsychotics have been associated with metabolic changes, including hyperglycemia, diabetic ketoacidosis, hyperosmolar, hyperglycemic states, and diabetic coma. Aggravation of diabetes mellitus has been reported. Possible mechanisms include atypical antipsychotic-induced insulin resistance or direct beta-cell inhibition.
Aspirin, ASA: (Moderate) Monitor blood glucose during concomitant sulfonylurea and aspirin use. Concomitant use may cause an increased blood glucose-lowering effect with risk of hypoglycemia.
Aspirin, ASA; Butalbital; Caffeine: (Moderate) Monitor blood glucose during concomitant sulfonylurea and aspirin use. Concomitant use may cause an increased blood glucose-lowering effect with risk of hypoglycemia.
Aspirin, ASA; Butalbital; Caffeine; Codeine: (Moderate) Monitor blood glucose during concomitant sulfonylurea and aspirin use. Concomitant use may cause an increased blood glucose-lowering effect with risk of hypoglycemia.
Aspirin, ASA; Caffeine: (Moderate) Monitor blood glucose during concomitant sulfonylurea and aspirin use. Concomitant use may cause an increased blood glucose-lowering effect with risk of hypoglycemia.
Aspirin, ASA; Caffeine; Dihydrocodeine: (Moderate) Monitor blood glucose during concomitant sulfonylurea and aspirin use. Concomitant use may cause an increased blood glucose-lowering effect with risk of hypoglycemia.
Aspirin, ASA; Caffeine; Orphenadrine: (Moderate) Monitor blood glucose during concomitant sulfonylurea and aspirin use. Concomitant use may cause an increased blood glucose-lowering effect with risk of hypoglycemia.
Aspirin, ASA; Carisoprodol: (Moderate) Monitor blood glucose during concomitant sulfonylurea and aspirin use. Concomitant use may cause an increased blood glucose-lowering effect with risk of hypoglycemia.
Aspirin, ASA; Carisoprodol; Codeine: (Moderate) Monitor blood glucose during concomitant sulfonylurea and aspirin use. Concomitant use may cause an increased blood glucose-lowering effect with risk of hypoglycemia.
Aspirin, ASA; Citric Acid; Sodium Bicarbonate: (Moderate) Monitor blood glucose during concomitant sulfonylurea and aspirin use. Concomitant use may cause an increased blood glucose-lowering effect with risk of hypoglycemia.
Aspirin, ASA; Dipyridamole: (Moderate) Monitor blood glucose during concomitant sulfonylurea and aspirin use. Concomitant use may cause an increased blood glucose-lowering effect with risk of hypoglycemia.
Aspirin, ASA; Omeprazole: (Moderate) Monitor blood glucose during concomitant sulfonylurea and aspirin use. Concomitant use may cause an increased blood glucose-lowering effect with risk of hypoglycemia.
Aspirin, ASA; Oxycodone: (Moderate) Monitor blood glucose during concomitant sulfonylurea and aspirin use. Concomitant use may cause an increased blood glucose-lowering effect with risk of

hypoglycemia.
Aspirin, ASA; Pravastatin: (Moderate) Monitor blood glucose during concomitant sulfonylurea and aspirin use. Concomitant use may cause an increased blood glucose-lowering effect with risk of hypoglycemia.
Atazanavir: (Moderate) New onset diabetes mellitus, exacerbation of diabetes mellitus, and hyperglycemia due to insulin resistance have been reported with use of anti-retroviral protease inhibitors. A possible mechanism is impairment of beta-cell function. Onset averaged approximately 63 days after initiating protease inhibitor therapy, but has occurred as early as 4 days after beginning therapy. Diabetic ketoacidosis has occurred in some patients including patients who were not diabetic prior to protease inhibitor treatment. Patients on antidiabetic agents should be closely monitored for changes in glycemic control, specifically hyperglycemia, if protease inhibitor therapy is initiated.
Atazanavir; Cobicistat: (Moderate) New onset diabetes mellitus, exacerbation of diabetes mellitus, and hyperglycemia due to insulin resistance have been reported with use of anti-retroviral protease inhibitors. A possible mechanism is impairment of beta-cell function. Onset averaged approximately 63 days after initiating protease inhibitor therapy, but has occurred as early as 4 days after beginning therapy. Diabetic ketoacidosis has occurred in some patients including patients who were not diabetic prior to protease inhibitor treatment. Patients on antidiabetic agents should be closely monitored for changes in glycemic control, specifically hyperglycemia, if protease inhibitor therapy is initiated.
Atenolol: (Moderate) Increased frequency of blood glucose monitoring may be required when a beta blocker is given with antidiabetic agents. Since beta blockers inhibit the release of catecholamines, these medications may hide symptoms of hypoglycemia such as tremor, tachycardia, and blood pressure changes. Other symptoms, like headache, dizziness, nervousness, mood changes, or hunger are not blunted. Beta-blockers also exert complex actions on the body's ability to regulate blood glucose. Some beta-blockers, particularly non-selective beta-blockers such as propranolol, have been noted to potentiate insulin-induced hypoglycemia and a delay in recovery of blood glucose to normal levels. Hyperglycemia has been reported as well and is possibly due to beta-2 receptor blockade in the beta cells of the pancreas. A selective beta-blocker may be preferred in patients with diabetes mellitus, if appropriate for the patient's condition. Selective beta-blockers, such as atenolol or metoprolol, do not appear to potentiate insulin-induced hypoglycemia. While beta-blockers may have negative effects on glycemic control, they reduce the risk of cardiovascular disease and stroke in patients with diabetes and their use should not be avoided in patients with compelling indications for beta-blocker therapy when no other contraindications are present.
Atenolol; Chlorthalidone: (Moderate) Increased frequency of blood glucose monitoring may be required when a beta blocker is given with antidiabetic agents. Since beta blockers inhibit the release of catecholamines, these medications may hide symptoms of hypoglycemia such as tremor, tachycardia, and blood pressure changes. Other symptoms, like headache, dizziness, nervousness, mood changes, or hunger are not blunted. Beta-blockers also exert complex actions on the body's ability to regulate blood glucose. Some beta-blockers, particularly non-selective beta-blockers such as propranolol, have been noted to potentiate insulin-induced hypoglycemia and a delay in recovery of blood glucose to normal levels. Hyperglycemia has been reported as well and is possibly due to beta-2 receptor blockade in the beta cells of the pancreas. A selective beta-blocker may be preferred in patients with diabetes mellitus, if appropriate for the patient's condition. Selective beta-blockers, such as atenolol or metoprolol, do not appear to potentiate insulin-induced hypoglycemia. While beta-blockers may have negative effects on glycemic control, they reduce the risk of cardiovascular disease and stroke in patients with diabetes and their use should not be avoided in patients with compelling indications for beta-blocker therapy when no other contraindications are present.
atypical antipsychotic: (Moderate) Atypical antipsychotic therapy may aggravate diabetes mellitus and cause metabolic changes such as hyperglycemia. Monitor patients on antidiabetic agents for worsening glycemic control. The atypical antipsychotics have been associated with metabolic changes, including

hyperglycemia, diabetic ketoacidosis, hyperosmolar, hyperglycemic states, and diabetic coma.
Aggravation of diabetes mellitus has been reported. Possible mechanisms include atypical antipsychotic-induced insulin resistance or direct beta-cell inhibition.
Azilsartan: (Moderate) Monitor blood glucose during concomitant sulfonylurea and angiotensin receptor blocker use. Concomitant use may cause an increased blood glucose-lowering effect with risk of hypoglycemia.
Azilsartan; Chlorthalidone: (Moderate) Monitor blood glucose during concomitant sulfonylurea and angiotensin receptor blocker use. Concomitant use may cause an increased blood glucose-lowering effect with risk of hypoglycemia.
Benazepril: (Moderate) Monitor blood glucose during concomitant sulfonylurea and angiotensin-converting enzyme (ACE) inhibitor use. Concomitant use may cause an increased blood glucose-lowering effect with risk of hypoglycemia.
Benazepril; Hydrochlorothiazide, HCTZ: (Moderate) Monitor blood glucose during concomitant sulfonylurea and angiotensin-converting enzyme (ACE) inhibitor use. Concomitant use may cause an increased blood glucose-lowering effect with risk of hypoglycemia.
Bendroflumethiazide; Nadolol: (Moderate) Increased frequency of blood glucose monitoring may be required when a beta blocker is given with antidiabetic agents. Since beta blockers inhibit the release of catecholamines, these medications may hide symptoms of hypoglycemia such as tremor, tachycardia, and blood pressure changes. Other symptoms, like headache, dizziness, nervousness, mood changes, or hunger are not blunted. Beta-blockers also exert complex actions on the body's ability to regulate blood glucose. Some beta-blockers, particularly non-selective beta-blockers such as propranolol, have been noted to potentiate insulin-induced hypoglycemia and a delay in recovery of blood glucose to normal levels. Hyperglycemia has been reported as well and is possibly due to beta-2 receptor blockade in the beta cells of the pancreas. A selective beta-blocker may be preferred in patients with diabetes mellitus, if appropriate for the patient's condition. Selective beta-blockers, such as atenolol or metoprolol, do not appear to potentiate insulin-induced hypoglycemia. While beta-blockers may have negative effects on glycemic control, they reduce the risk of cardiovascular disease and stroke in patients with diabetes and their use should not be avoided in patients with compelling indications for beta-blocker therapy when no other contraindications are present.
Benzphetamine: (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.
Beta-blockers: (Moderate) Increased frequency of blood glucose monitoring may be required when a beta blocker is given with antidiabetic agents. Since beta blockers inhibit the release of catecholamines, these medications may hide symptoms of hypoglycemia such as tremor, tachycardia, and blood pressure changes. Other symptoms, like headache, dizziness, nervousness, mood changes, or hunger are not blunted. Beta-blockers also exert complex actions on the body's ability to regulate blood glucose. Some beta-blockers, particularly non-selective beta-blockers such as propranolol, have been noted to potentiate insulin-induced hypoglycemia and a delay in recovery of blood glucose to normal levels. Hyperglycemia has been reported as well and is possibly due to beta-2 receptor blockade in the beta cells of the pancreas. A selective beta-blocker may be preferred in patients with diabetes mellitus, if appropriate for the patient's condition. Selective beta-blockers, such as atenolol or metoprolol, do not appear to potentiate insulin-induced hypoglycemia. While beta-blockers may have negative effects on glycemic control, they reduce

the risk of cardiovascular disease and stroke in patients with diabetes and their use should not be avoided in patients with compelling indications for beta-blocker therapy when no other contraindications are present.
Betaxolol: (Moderate) Increased frequency of blood glucose monitoring may be required when a beta blocker is given with antidiabetic agents. Since beta blockers inhibit the release of catecholamines, these medications may hide symptoms of hypoglycemia such as tremor, tachycardia, and blood pressure changes. Other symptoms, like headache, dizziness, nervousness, mood changes, or hunger are not blunted. Beta-blockers also exert complex actions on the body's ability to regulate blood glucose. Some beta-blockers, particularly non-selective beta-blockers such as propranolol, have been noted to potentiate insulin-induced hypoglycemia and a delay in recovery of blood glucose to normal levels. Hyperglycemia has been reported as well and is possibly due to beta-2 receptor blockade in the beta cells of the pancreas. A selective beta-blocker may be preferred in patients with diabetes mellitus, if appropriate for the patient's condition. Selective beta-blockers, such as atenolol or metoprolol, do not appear to potentiate insulin-induced hypoglycemia. While beta-blockers may have negative effects on glycemic control, they reduce the risk of cardiovascular disease and stroke in patients with diabetes and their use should not be avoided in patients with compelling indications for beta-blocker therapy when no other contraindications are present.
Bexarotene: (Moderate) Systemic bexarotene may enhance the action of agents that enhance insulin secretion (e.g., sulfonylureas) resulting in hypoglycemia. Patients should be closely monitored while receiving bexarotene capsules in combination with any of these agents; monitor for hypoglycemia and the need for diabetic therapy adjustments. Hypoglycemia has not been associated with bexarotene monotherapy.
Bismuth Subcitrate Potassium; Metronidazole; Tetracycline: (Moderate) Additive photosensitization may be seen with concurrent administration of sulfonylureas and other photosensitizing agents including tetracyclines. Prevention of photosensitivity includes adequate protection from sources of UV radiation (e.g., avoiding sun exposure and tanning booths) and the use of protective clothing and sunscreens on exposed skin.
Bismuth Subsalicylate: (Moderate) If salicylates and sulfonylureas are to be administered together, patients should be monitored for changes in glycemic control. Salicylates, by inhibiting prostaglandin E2 synthesis, can indirectly increase insulin secretion. Thus, salicylates can decrease blood sugar and may potentiate the effects of other antidiabetic agents. This mechanism may explain how salicylates can potentiate the clinical effects of sulfonylureas; however, displacement of sulfonylureas from protein binding sites has also been reported. In large doses, salicylates uncouple oxidative phosphorylation, deplete hepatic and muscle glycogen, and cause hyperglycemia and glycosuria.
Bismuth Subsalicylate; Metronidazole; Tetracycline: (Moderate) Additive photosensitization may be seen with concurrent administration of sulfonylureas and other photosensitizing agents including tetracyclines. Prevention of photosensitivity includes adequate protection from sources of UV radiation (e.g., avoiding sun exposure and tanning booths) and the use of protective clothing and sunscreens on exposed skin. (Moderate) If salicylates and sulfonylureas are to be administered together, patients should be monitored for changes in glycemic control. Salicylates, by inhibiting prostaglandin E2 synthesis, can indirectly increase insulin secretion. Thus, salicylates can decrease blood sugar and may potentiate the effects of other antidiabetic agents. This mechanism may explain how salicylates can potentiate the clinical effects of sulfonylureas; however, displacement of sulfonylureas from protein binding sites has also been reported. In large doses, salicylates uncouple oxidative phosphorylation, deplete hepatic and muscle glycogen, and cause hyperglycemia and glycosuria.
Bisoprolol: (Moderate) Increased frequency of blood glucose monitoring may be required when a beta blocker is given with antidiabetic agents. Since beta blockers inhibit the release of catecholamines, these medications may hide symptoms of hypoglycemia such as tremor, tachycardia, and blood pressure

changes. Other symptoms, like headache, dizziness, nervousness, mood changes, or hunger are not blunted. Beta-blockers also exert complex actions on the body's ability to regulate blood glucose. Some beta-blockers, particularly non-selective beta-blockers such as propranolol, have been noted to potentiate insulin-induced hypoglycemia and a delay in recovery of blood glucose to normal levels. Hyperglycemia has been reported as well and is possibly due to beta-2 receptor blockade in the beta cells of the pancreas. A selective beta-blocker may be preferred in patients with diabetes mellitus, if appropriate for the patient's condition. Selective beta-blockers, such as atenolol or metoprolol, do not appear to potentiate insulin-induced hypoglycemia. While beta-blockers may have negative effects on glycemic control, they reduce the risk of cardiovascular disease and stroke in patients with diabetes and their use should not be avoided in patients with compelling indications for beta-blocker therapy when no other contraindications are present.

Bisoprolol; Hydrochlorothiazide, HCTZ: (Moderate) Increased frequency of blood glucose monitoring may be required when a beta blocker is given with antidiabetic agents. Since beta blockers inhibit the release of catecholamines, these medications may hide symptoms of hypoglycemia such as tremor, tachycardia, and blood pressure changes. Other symptoms, like headache, dizziness, nervousness, mood changes, or hunger are not blunted. Beta-blockers also exert complex actions on the body's ability to regulate blood glucose. Some beta-blockers, particularly non-selective beta-blockers such as propranolol, have been noted to potentiate insulin-induced hypoglycemia and a delay in recovery of blood glucose to normal levels. Hyperglycemia has been reported as well and is possibly due to beta-2 receptor blockade in the beta cells of the pancreas. A selective beta-blocker may be preferred in patients with diabetes mellitus, if appropriate for the patient's condition. Selective beta-blockers, such as atenolol or metoprolol, do not appear to potentiate insulin-induced hypoglycemia. While beta-blockers may have negative effects on glycemic control, they reduce the risk of cardiovascular disease and stroke in patients with diabetes and their use should not be avoided in patients with compelling indications for beta-blocker therapy when no other contraindications are present.

Bortezomib: (Moderate) During clinical trials of bortezomib, hypoglycemia and hyperglycemia were reported in diabetic patients receiving antidiabetic agents. Patients taking antidiabetic agents and receiving bortezomib treatment may require close monitoring of their blood glucose levels and dosage adjustment of their medication.

Brexpiprazole: (Moderate) Atypical antipsychotic therapy may aggravate diabetes mellitus and cause metabolic changes such as hyperglycemia. Monitor patients on antidiabetic agents for worsening glycemic control. The atypical antipsychotics have been associated with metabolic changes, including hyperglycemia, diabetic ketoacidosis, hyperosmolar, hyperglycemic states, and diabetic coma. Aggravation of diabetes mellitus has been reported. Possible mechanisms include atypical antipsychotic-induced insulin resistance or direct beta-cell inhibition.

Brimonidine; Timolol: (Moderate) Increased frequency of blood glucose monitoring may be required when a beta blocker is given with antidiabetic agents. Since beta blockers inhibit the release of catecholamines, these medications may hide symptoms of hypoglycemia such as tremor, tachycardia, and blood pressure changes. Other symptoms, like headache, dizziness, nervousness, mood changes, or hunger are not blunted. Beta-blockers also exert complex actions on the body's ability to regulate blood glucose. Some beta-blockers, particularly non-selective beta-blockers such as propranolol, have been noted to potentiate insulin-induced hypoglycemia and a delay in recovery of blood glucose to normal levels. Hyperglycemia has been reported as well and is possibly due to beta-2 receptor blockade in the beta cells of the pancreas. A selective beta-blocker may be preferred in patients with diabetes mellitus, if appropriate for the patient's condition. Selective beta-blockers, such as atenolol or metoprolol, do not appear to potentiate insulin-induced hypoglycemia. While beta-blockers may have negative effects on glycemic control, they reduce the risk of cardiovascular disease and stroke in patients with diabetes and their use should not be avoided in patients with compelling indications for beta-blocker therapy when no other contraindications are

present.
Brompheniramine; Carbetapentane; Phenylephrine: (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.
Brompheniramine; Dextromethorphan; Phenylephrine: (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.
Brompheniramine; Hydrocodone; Pseudoephedrine: (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.
Brompheniramine; Phenylephrine: (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.
Brompheniramine; Pseudoephedrine: (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.
Brompheniramine; Pseudoephedrine; Dextromethorphan: (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.
Bumetanide: (Minor) Bumetanide has been associated with hyperglycemia, possibly due to potassium depletion, and, glycosuria has been reported. Because of this, a potential pharmacodynamic interaction exists between bumetanide and all antidiabetic agents. This interference can lead to a loss of diabetic control, so diabetic patients should be monitored closely.
Bupivacaine; Epinephrine: (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) Monitor blood glucose during concomitant sulfonylurea and metformin use; a sulfonylurea dose adjustment may be necessary. Concomitant use may cause an increased blood glucose-lowering effect with risk of hypoglycemia.
Candesartan: (Moderate) Monitor blood glucose during concomitant sulfonylurea and angiotensin receptor blocker use. Concomitant use may cause an increased blood glucose-lowering effect with risk of hypoglycemia.
Candesartan; Hydrochlorothiazide, HCTZ: (Moderate) Monitor blood glucose during concomitant sulfonylurea and angiotensin receptor blocker use. Concomitant use may cause an increased blood glucose-lowering effect with risk of hypoglycemia.
Captopril: (Moderate) Monitor blood glucose during concomitant sulfonylurea and angiotensin-converting enzyme (ACE) inhibitor use. Concomitant use may cause an increased blood glucose-lowering effect with risk of hypoglycemia.
Captopril; Hydrochlorothiazide, HCTZ: (Moderate) Monitor blood glucose during concomitant sulfonylurea and angiotensin-converting enzyme (ACE) inhibitor use. Concomitant use may cause an increased blood glucose-lowering effect with risk of hypoglycemia.
Carbetapentane; Chlorpheniramine; Phenylephrine: (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.
Carbetapentane; Diphenhydramine; Phenylephrine: (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.
Carbetapentane; Guaifenesin; Phenylephrine: (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.
Carbetapentane; Phenylephrine: (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.
Carbetapentane; Phenylephrine; Pyrilamine: (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.
Carbetapentane; Pseudoephedrine: (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.
Carbinoxamine; Dextromethorphan; Pseudoephedrine: (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.
Carbinoxamine; Hydrocodone; Phenylephrine: (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.
Carbinoxamine; Hydrocodone; Pseudoephedrine: (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.
Carbinoxamine; Phenylephrine: (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.
Carbinoxamine; Pseudoephedrine: (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.
Carbonic anhydrase inhibitors: (Minor) Carbonic anhydrase inhibitors may alter blood sugar. Both hyperglycemia and hypoglycemia have been described in patients treated with acetazolamide. This should be taken into consideration in patients with impaired glucose tolerance or diabetes mellitus who are receiving antidiabetic agents. Monitor blood glucose and for changes in glycemic control and be alert for evidence of an interaction.
Cariprazine: (Moderate) Atypical antipsychotic therapy may aggravate diabetes mellitus and cause metabolic changes such as hyperglycemia. Monitor patients on antidiabetic agents for worsening glycemic control. The atypical antipsychotics have been associated with metabolic changes, including hyperglycemia, diabetic ketoacidosis, hyperosmolar, hyperglycemic states, and diabetic coma. Aggravation of diabetes mellitus has been reported. Possible mechanisms include atypical antipsychotic-induced insulin resistance or direct beta-cell inhibition.
Carteolol: (Moderate) Increased frequency of blood glucose monitoring may be required when a beta blocker is given with antidiabetic agents. Since beta blockers inhibit the release of catecholamines, these medications may hide symptoms of hypoglycemia such as tremor, tachycardia, and blood pressure changes. Other symptoms, like headache, dizziness, nervousness, mood changes, or hunger are not blunted. Beta-blockers also exert complex actions on the body's ability to regulate blood glucose. Some beta-blockers, particularly non-selective beta-blockers such as propranolol, have been noted to potentiate insulin-induced hypoglycemia and a delay in recovery of blood glucose to normal levels. Hyperglycemia has been reported as well and is possibly due to beta-2 receptor blockade in the beta cells of the pancreas. A selective beta-blocker may be preferred in patients with diabetes mellitus, if appropriate for the patient's condition. Selective beta-blockers, such as atenolol or metoprolol, do not appear to potentiate insulin-induced hypoglycemia. While beta-blockers may have negative effects on glycemic control, they reduce the risk of cardiovascular disease and stroke in patients with diabetes and their use should not be avoided in patients with compelling indications for beta-blocker therapy when no other contraindications are present.
Carvedilol: (Moderate) Increased frequency of blood glucose monitoring may be required when a beta blocker is given with antidiabetic agents. Since beta blockers inhibit the release of catecholamines, these medications may hide symptoms of hypoglycemia such as tremor, tachycardia, and blood pressure

changes. Other symptoms, like headache, dizziness, nervousness, mood changes, or hunger are not blunted. Beta-blockers also exert complex actions on the body's ability to regulate blood glucose. Some beta-blockers, particularly non-selective beta-blockers such as propranolol, have been noted to potentiate insulin-induced hypoglycemia and a delay in recovery of blood glucose to normal levels. Hyperglycemia has been reported as well and is possibly due to beta-2 receptor blockade in the beta cells of the pancreas. A selective beta-blocker may be preferred in patients with diabetes mellitus, if appropriate for the patient's condition. Selective beta-blockers, such as atenolol or metoprolol, do not appear to potentiate insulin-induced hypoglycemia. While beta-blockers may have negative effects on glycemic control, they reduce the risk of cardiovascular disease and stroke in patients with diabetes and their use should not be avoided in patients with compelling indications for beta-blocker therapy when no other contraindications are present.

Cetirizine; Pseudoephedrine: (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.

Chlophedianol; Dexchlorpheniramine; Pseudoephedrine: (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.

Chlophedianol; Guaifenesin; Phenylephrine: (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.

Chloramphenicol: (Moderate) Clinical hypoglycemia may be observed when chloramphenicol is used in combination with sulfonylureas. If chloramphenicol is administered or discontinued in patients receiving oral sulfonylureas, patients should be monitored for hypoglycemia or loss of blood glucose control. Chloramphenicol may inhibit the hepatic metabolism of sulfonylureas. In addition, the hypoglycemic action of glyburide and glipizide may be potentiated by other drugs that are highly protein bound, such as chloramphenicol.

Chloroquine: (Major) Careful monitoring of blood glucose is recommended when chloroquine and antidiabetic agents, including the sulfonylureas, are coadministered. A decreased dose of the antidiabetic agent may be necessary as severe hypoglycemia has been reported in patients treated concomitantly with chloroquine and an antidiabetic agent.

Chlorpheniramine; Dextromethorphan; Phenylephrine: (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.
Chlorpheniramine; Dextromethorphan; Pseudoephedrine: (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.
Chlorpheniramine; Dihydrocodeine; Phenylephrine: (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.
Chlorpheniramine; Dihydrocodeine; Pseudoephedrine: (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.
Chlorpheniramine; Guaifenesin; Hydrocodone; Pseudoephedrine: (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.
Chlorpheniramine; Hydrocodone; Phenylephrine: (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.
Chlorpheniramine; Hydrocodone; Pseudoephedrine: (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.
Chlorpheniramine; Ibuprofen; Pseudoephedrine: (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.
Chlorpheniramine; Phenylephrine: (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.
Chlorpheniramine; Pseudoephedrine: (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.
Chlorthalidone; Clonidine: (Minor) Increased frequency of blood glucose monitoring may be required when clonidine is given with antidiabetic agents. Since clonidine inhibits the release of catecholamines, clonidine may hide symptoms of hypoglycemia such as tremor, tachycardia, and blood pressure changes. Other symptoms, like headache, dizziness, nervousness, mood changes, or hunger are not blunted. Clonidine does not appear to impair recovery from hypoglycemia, and has not been found to impair glucose tolerance in diabetic patients.
Choline Salicylate; Magnesium Salicylate: (Moderate) If salicylates and sulfonylureas are to be administered together, patients should be monitored for changes in glycemic control. Salicylates, by inhibiting prostaglandin E2 synthesis, can indirectly increase insulin secretion. Thus, salicylates can decrease blood sugar and may potentiate the effects of other antidiabetic agents. This mechanism may explain how salicylates can potentiate the clinical effects of sulfonylureas; however, displacement of sulfonylureas from protein binding sites has also been reported. In large doses, salicylates uncouple oxidative phosphorylation, deplete hepatic and muscle glycogen, and cause hyperglycemia and glycosuria.
Chromium: (Moderate) Chromium dietary supplements may lower blood glucose. As part of the glucose tolerance factor molecule, chromium appears to facilitate the binding of insulin to insulin receptors in tissues and to aid in glucose metabolism. Because blood glucose may be lowered by the use of chromium, patients who are on antidiabetic agents may need dose adjustments. Close monitoring of blood glucose is recommended.
Cimetidine: (Moderate) Cimetidine has been shown to affect the pharmacokinetics of some oral

sulfonylureas. Patients receiving sulfonylureas should be observed for evidence of altered glycemic response when cimetidine is instituted or discontinued. The mechanism of this interaction may involve either increasing the absorption or decreasing the clearance of the sulfonylurea. Asymptomatic hypoglycemia has been observed as a result of this interaction. It is unclear at this time if famotidine or nizatidine interact with oral sulfonylureas.
Cisapride: (Moderate) Because cisapride can enhance gastric emptying in diabetic patients, blood glucose can be affected, which, in turn, may affect the clinical response to antidiabetic agents. Monitor blood glucose and adjust if cliniically indicated.
Citric Acid; Potassium Citrate; Sodium Citrate: (Moderate) Urinary alkalinizing agents, like potassium citrate, may increase the excretion of chlorpropamide by increasing renal clearance. Monitor for decreased efficacy of chlorpropamide (i.e., increased blood glucose) during coadministration.
Clarithromycin: (Moderate) The concomitant use of clarithromycin and antidiabetic agents can result in significant hypoglycemia. Careful monitoring of blood glucose is recommended.
Clindamycin; Tretinoin: (Moderate) A manufacturer of topical tretinoin states that tretinoin, ATRA should be administered with caution in patients who are also taking drugs known to be photosensitizers, such as sulfonylureas, as concomitant use may augment phototoxicity. Patients should take care and use proper techniques to limit sunlight and UV exposure of treated areas.
Clonidine: (Minor) Increased frequency of blood glucose monitoring may be required when clonidine is given with antidiabetic agents. Since clonidine inhibits the release of catecholamines, clonidine may hide symptoms of hypoglycemia such as tremor, tachycardia, and blood pressure changes. Other symptoms, like headache, dizziness, nervousness, mood changes, or hunger are not blunted. Clonidine does not appear to impair recovery from hypoglycemia, and has not been found to impair glucose tolerance in diabetic patients.
Clozapine: (Moderate) Atypical antipsychotic therapy may aggravate diabetes mellitus and cause metabolic changes such as hyperglycemia. Monitor patients on antidiabetic agents for worsening glycemic control. The atypical antipsychotics have been associated with metabolic changes, including hyperglycemia, diabetic ketoacidosis, hyperosmolar, hyperglycemic states, and diabetic coma. Aggravation of diabetes mellitus has been reported. Possible mechanisms include atypical antipsychotic-induced insulin resistance or direct beta-cell inhibition.
Codeine; Guaifenesin; Pseudoephedrine: (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.
Codeine; Phenylephrine; Promethazine: (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.
Colesevelam: (Moderate) Colesevelam reduces the oral bioavailability of glyburide, glipizide, glimepiride and other sulfonylureas. Administer these drugs at least 4 hours before colesevelam to limit this interaction. Drug response, including glycemic control, should also be monitored. Additionally, in patients

with type 2 diabetes mellitus receiving sulfonylureas, colesevelam increased serum triglyceride concentrations by 18% compared to placebo (p less than 0.001). Monitor patients taking these treatments together for an increase in triglyceride concentrations. Discontinue colesevelam if triglyceride concentrations are more than 500 mg/dL or if hypertriglyceridemia-induced pancreatitis occurs.
Conjugated Estrogens: (Minor) Patients receiving antidiabetic agents should be periodically monitored for changes in glycemic control when hormone therapy is instituted or discontinued. Estrogens can decrease the hypoglycemic effects of antidiabetic agents by impairing glucose tolerance. Changes in glucose tolerance occur more commonly in patients receiving 50 mcg or more of ethinyl estradiol (or equivalent) per day in combined oral contraceptives (COCs), which are not commonly used in practice since the marketing of lower dose COCs, patches, injections and rings. The presence or absence of a concomitant progestin may influence the significance of any hormonal effect on glucose homeostasis.
Conjugated Estrogens; Bazedoxifene: (Minor) Patients receiving antidiabetic agents should be periodically monitored for changes in glycemic control when hormone therapy is instituted or discontinued. Estrogens can decrease the hypoglycemic effects of antidiabetic agents by impairing glucose tolerance. Changes in glucose tolerance occur more commonly in patients receiving 50 mcg or more of ethinyl estradiol (or equivalent) per day in combined oral contraceptives (COCs), which are not commonly used in practice since the marketing of lower dose COCs, patches, injections and rings. The presence or absence of a concomitant progestin may influence the significance of any hormonal effect on glucose homeostasis.
Conjugated Estrogens; Medroxyprogesterone: (Minor) Patients receiving antidiabetic agents should be periodically monitored for changes in glycemic control when hormone therapy is instituted or discontinued. Estrogens can decrease the hypoglycemic effects of antidiabetic agents by impairing glucose tolerance. Changes in glucose tolerance occur more commonly in patients receiving 50 mcg or more of ethinyl estradiol (or equivalent) per day in combined oral contraceptives (COCs), which are not commonly used in practice since the marketing of lower dose COCs, patches, injections and rings. The presence or absence of a concomitant progestin may influence the significance of any hormonal effect on glucose homeostasis.
Corticosteroids: (Moderate) Monitor blood glucose during concomitant corticosteroid and sulfonylurea use; a sulfonylurea dose adjustment may be necessary. Corticosteroids may increase blood glucose concentrations. Risk factors for impaired glucose tolerance due to corticosteroids include the corticosteroid dose and duration of treatment. Corticosteroids stimulate hepatic glucose production and inhibit peripheral glucose uptake into muscle and fatty tissues, producing insulin resistance. Decreased insulin production may occur in the pancreas due to a direct effect on pancreatic beta cells.
Cyclosporine: (Moderate) Sulfonylureas may increase concentrations of cyclosporine. Retrospective data from 6 adults with post-renal transplant diabetes mellitus and normal hepatic and renal function before and after glyburide initiation were examined. The mean plasma cyclosporine concentration from 5 months of data before glyburide use was 212.3 +/- 66.4 ng/ml. In contrast, the mean plasma cyclosporine concentration from 5 months of data during glyburide use was 334.8 +/- 65.8 ng/ml. Until more data are available, when glyburide is added to cyclosporine therapy, monitor cyclosporine concentrations and adjust cyclosporine dosage as necessary. Also, monitor patients for increased cyclosporine toxicity (renal dysfunction, neurotoxicity). In addition, cyclosporine has been reported to cause hyperglycemia. Cyclosporine may have direct beta-cell toxicity, the effects of which may be dose-related. Patients should be monitored for worsening of glycemic control if cyclosporine is initiated in patients receiving antidiabetic agents.
Daclatasvir: (Moderate) Closely monitor blood glucose levels if daclatasvir is administered with antidiabetic agents. Dose adjustments of the antidiabetic agents may be needed. Altered blood glucose control, resulting in serious symptomatic hypoglycemia, has been reported in diabetic patients receiving antidiabetic agents in combination with direct acting antivirals, such as daclatasvir.
Danazol: (Moderate) Changes in insulin sensitivity or glycemic control may occur in patients treated with

androgens. In diabetic patients, the metabolic effects of androgens may decrease blood glucose and, therefore, may decrease antidiabetic agent dosage requirements. Monitor blood glucose and HbA1C when these drugs are used together.
Dapagliflozin; Metformin: (Moderate) Monitor blood glucose during concomitant sulfonylurea and metformin use; a sulfonylurea dose adjustment may be necessary. Concomitant use may cause an increased blood glucose-lowering effect with risk of hypoglycemia.
Dapagliflozin; Saxagliptin: (Moderate) A lower sulfonylurea dose may be required when used in combination with saxagliptin to minimize the risk of hypoglycemia. When saxagliptin was used in combination with a sulfonylurea, the incidence of hypoglycemia was increased compared to a placebo used in combination with a sulfonylurea.
Darunavir: (Moderate) New onset diabetes mellitus, exacerbation of diabetes mellitus, and hyperglycemia due to insulin resistance have been reported with use of anti-retroviral protease inhibitors. A possible mechanism is impairment of beta-cell function. Onset averaged approximately 63 days after initiating protease inhibitor therapy, but has occurred as early as 4 days after beginning therapy. Diabetic ketoacidosis has occurred in some patients including patients who were not diabetic prior to protease inhibitor treatment. Patients on antidiabetic agents should be closely monitored for changes in glycemic control, specifically hyperglycemia, if protease inhibitor therapy is initiated.
Darunavir; Cobicistat: (Moderate) New onset diabetes mellitus, exacerbation of diabetes mellitus, and hyperglycemia due to insulin resistance have been reported with use of anti-retroviral protease inhibitors. A possible mechanism is impairment of beta-cell function. Onset averaged approximately 63 days after initiating protease inhibitor therapy, but has occurred as early as 4 days after beginning therapy. Diabetic ketoacidosis has occurred in some patients including patients who were not diabetic prior to protease inhibitor treatment. Patients on antidiabetic agents should be closely monitored for changes in glycemic control, specifically hyperglycemia, if protease inhibitor therapy is initiated.
Darunavir; Cobicistat; Emtricitabine; Tenofovir alafenamide: (Moderate) New onset diabetes mellitus, exacerbation of diabetes mellitus, and hyperglycemia due to insulin resistance have been reported with use of anti-retroviral protease inhibitors. A possible mechanism is impairment of beta-cell function. Onset averaged approximately 63 days after initiating protease inhibitor therapy, but has occurred as early as 4 days after beginning therapy. Diabetic ketoacidosis has occurred in some patients including patients who were not diabetic prior to protease inhibitor treatment. Patients on antidiabetic agents should be closely monitored for changes in glycemic control, specifically hyperglycemia, if protease inhibitor therapy is initiated.
Dasabuvir; Ombitasvir; Paritaprevir; Ritonavir : (Moderate) Closely monitor blood glucose levels if dasabuvir; ombitasvir; paritaprevir; ritonavir is administered with antidiabetic agents. Dose adjustments of the antidiabetic agents may be needed. Altered blood glucose control, resulting in serious symptomatic hypoglycemia, has been reported in diabetic patients receiving antidiabetic agents in combination with direct acting antivirals, such as dasabuvir; ombitasvir; paritaprevir; ritonavir.
Dasabuvir; Ombitasvir; Paritaprevir; Ritonavir: (Moderate) New onset diabetes mellitus, exacerbation of diabetes mellitus, and hyperglycemia due to insulin resistance have been reported with use of anti-retroviral protease inhibitors. A possible mechanism is impairment of beta-cell function. Onset averaged approximately 63 days after initiating protease inhibitor therapy, but has occurred as early as 4 days after beginning therapy. Diabetic ketoacidosis has occurred in some patients including patients who were not diabetic prior to protease inhibitor treatment. Patients on antidiabetic agents should be closely monitored for changes in glycemic control, specifically hyperglycemia, if protease inhibitor therapy is initiated.
Demeclocycline: (Moderate) Additive photosensitization may be seen with concurrent administration of sulfonylureas and other photosensitizing agents including tetracyclines. Prevention of photosensitivity includes adequate protection from sources of UV radiation (e.g., avoiding sun exposure and tanning booths) and the use of protective clothing and sunscreens on exposed skin.

Desloratadine; Pseudoephedrine: (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.
Desmopressin: (Moderate) Additive hyponatremic effects may be seen in patients treated with desmopressin and drugs associated with SIADH including chlorpropamide. Use this combination with caution, and monitor patients for signs and symptoms of hyponatremia. Although rare, chlorpropamide has caused a reaction identical to symptom of inappropriate antidiuretic hormone (SIADH).
Desogestrel; Ethinyl Estradiol: (Minor) Patients receiving antidiabetic agents should be periodically monitored for changes in glycemic control when hormone therapy is instituted or discontinued. Estrogens can decrease the hypoglycemic effects of antidiabetic agents by impairing glucose tolerance. Changes in glucose tolerance occur more commonly in patients receiving 50 mcg or more of ethinyl estradiol (or equivalent) per day in combined oral contraceptives (COCs), which are not commonly used in practice since the marketing of lower dose COCs, patches, injections and rings. The presence or absence of a concomitant progestin may influence the significance of any hormonal effect on glucose homeostasis.
Dexbrompheniramine; Pseudoephedrine: (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.
Dexchlorpheniramine; Dextromethorphan; Pseudoephedrine: (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.
Dexmethylphenidate: (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.
Dextroamphetamine: (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.
Dextromethorphan; Diphenhydramine; Phenylephrine: (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.
Dextromethorphan; Guaifenesin; Phenylephrine: (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.
Dextromethorphan; Guaifenesin; Pseudoephedrine: (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.
Diazoxide: (Minor) Diazoxide, when administered intravenously or orally, produces a prompt dose-related increase in blood glucose level, due primarily to an inhibition of insulin release from the pancreas, and also to an extrapancreatic effect. The hyperglycemic effect begins within an hour and generally lasts no more than 8 hours in the presence of normal renal function. The hyperglycemic effect of diazoxide is expected to be antagonized by certain antidiabetic agents (e.g., insulin or a sulfonylurea). Blood glucose should be closely monitored.
Dienogest; Estradiol valerate: (Minor) Patients receiving antidiabetic agents should be periodically monitored for changes in glycemic control when hormone therapy is instituted or discontinued. Estrogens can decrease the hypoglycemic effects of antidiabetic agents by impairing glucose tolerance. Changes in glucose tolerance occur more commonly in patients receiving 50 mcg or more of ethinyl estradiol (or equivalent) per day in combined oral contraceptives (COCs), which are not commonly used in practice since the marketing of lower dose COCs, patches, injections and rings. The presence or absence of a concomitant progestin may influence the significance of any hormonal effect on glucose homeostasis.
Diethylpropion: (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.

Diethylstilbestrol, DES: (Minor) Patients receiving antidiabetic agents should be periodically monitored for changes in glycemic control when hormone therapy is instituted or discontinued. Estrogens can decrease the hypoglycemic effects of antidiabetic agents by impairing glucose tolerance. Changes in glucose tolerance occur more commonly in patients receiving 50 mcg or more of ethinyl estradiol (or equivalent) per day in combined oral contraceptives (COCs), which are not commonly used in practice since the marketing of lower dose COCs, patches, injections and rings. The presence or absence of a concomitant progestin may influence the significance of any hormonal effect on glucose homeostasis.
Difelikefalin: (Moderate) Monitor for dizziness, somnolence, mental status changes, and gait disturbances if concomitant use of difelikefalin with CNS depressants is necessary. Concomitant use may increase the risk for these adverse reactions.
Dihydrocodeine; Guaifenesin; Pseudoephedrine: (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) 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; Phenylephrine: (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.
Disopyramide: (Moderate) Disopyramide may enhance the hypoglycemic effects of antidiabetic agents. Patients receiving disopyramide concomitantly with antidiabetic agents should be monitored for changes in glycemic control.
Dobutamine: (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.
Dopamine: (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.
Dorzolamide; Timolol: (Moderate) Increased frequency of blood glucose monitoring may be required when a beta blocker is given with antidiabetic agents. Since beta blockers inhibit the release of catecholamines, these medications may hide symptoms of hypoglycemia such as tremor, tachycardia, and blood pressure changes. Other symptoms, like headache, dizziness, nervousness, mood changes, or hunger are not blunted. Beta-blockers also exert complex actions on the body's ability to regulate blood glucose. Some beta-blockers, particularly non-selective beta-blockers such as propranolol, have been noted to potentiate insulin-induced hypoglycemia and a delay in recovery of blood glucose to normal levels. Hyperglycemia has been reported as well and is possibly due to beta-2 receptor blockade in the beta cells of the pancreas. A selective beta-blocker may be preferred in patients with diabetes mellitus, if appropriate for the patient's condition. Selective beta-blockers, such as atenolol or metoprolol, do not appear to potentiate insulin-induced hypoglycemia. While beta-blockers may have negative effects on glycemic control, they reduce the risk of cardiovascular disease and stroke in patients with diabetes and their use should not be avoided in patients with compelling indications for beta-blocker therapy when no other contraindications are present.
Doxapram: (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.
Doxycycline: (Moderate) Additive photosensitization may be seen with concurrent administration of sulfonylureas and other photosensitizing agents including tetracyclines. Prevention of photosensitivity includes adequate protection from sources of UV radiation (e.g., avoiding sun exposure and tanning booths) and the use of protective clothing and sunscreens on exposed skin.
Drospirenone; Estetrol: (Minor) Patients receiving antidiabetic agents should be periodically monitored for changes in glycemic control when hormone therapy is instituted or discontinued. Estrogens can decrease the hypoglycemic effects of antidiabetic agents by impairing glucose tolerance. Changes in glucose tolerance occur more commonly in patients receiving 50 mcg or more of ethinyl estradiol (or equivalent) per day in combined oral contraceptives (COCs), which are not commonly used in practice since the marketing of lower dose COCs, patches, injections and rings. The presence or absence of a concomitant progestin may influence the significance of any hormonal effect on glucose homeostasis.
Drospirenone; Estradiol: (Minor) Patients receiving antidiabetic agents should be periodically monitored for changes in glycemic control when hormone therapy is instituted or discontinued. Estrogens can decrease the hypoglycemic effects of antidiabetic agents by impairing glucose tolerance. Changes in glucose tolerance occur more commonly in patients receiving 50 mcg or more of ethinyl estradiol (or equivalent) per day in combined oral contraceptives (COCs), which are not commonly used in practice since the marketing of lower dose COCs, patches, injections and rings. The presence or absence of a concomitant progestin may influence the significance of any hormonal effect on glucose homeostasis.
Drospirenone; Ethinyl Estradiol: (Minor) Patients receiving antidiabetic agents should be periodically monitored for changes in glycemic control when hormone therapy is instituted or discontinued. Estrogens can decrease the hypoglycemic effects of antidiabetic agents by impairing glucose tolerance. Changes in

glucose tolerance occur more commonly in patients receiving 50 mcg or more of ethinyl estradiol (or equivalent) per day in combined oral contraceptives (COCs), which are not commonly used in practice since the marketing of lower dose COCs, patches, injections and rings. The presence or absence of a concomitant progestin may influence the significance of any hormonal effect on glucose homeostasis.
Drospirenone; Ethinyl Estradiol; Levomefolate: (Minor) Patients receiving antidiabetic agents should be periodically monitored for changes in glycemic control when hormone therapy is instituted or discontinued. Estrogens can decrease the hypoglycemic effects of antidiabetic agents by impairing glucose tolerance. Changes in glucose tolerance occur more commonly in patients receiving 50 mcg or more of ethinyl estradiol (or equivalent) per day in combined oral contraceptives (COCs), which are not commonly used in practice since the marketing of lower dose COCs, patches, injections and rings. The presence or absence of a concomitant progestin may influence the significance of any hormonal effect on glucose homeostasis.
Dulaglutide: (Moderate) Monitor blood glucose during concomitant sulfonylurea and dulaglutide use; consider decreasing the sulfonylurea dose when starting dulaglutide. Concomitant use may cause an increased blood glucose-lowering effect with risk of hypoglycemia.
Elagolix; Estradiol; Norethindrone acetate: (Minor) Patients receiving antidiabetic agents should be periodically monitored for changes in glycemic control when hormone therapy is instituted or discontinued. Estrogens can decrease the hypoglycemic effects of antidiabetic agents by impairing glucose tolerance. Changes in glucose tolerance occur more commonly in patients receiving 50 mcg or more of ethinyl estradiol (or equivalent) per day in combined oral contraceptives (COCs), which are not commonly used in practice since the marketing of lower dose COCs, patches, injections and rings. The presence or absence of a concomitant progestin may influence the significance of any hormonal effect on glucose homeostasis.
Elbasvir; Grazoprevir: (Moderate) Closely monitor blood glucose levels if elbasvir is administered with antidiabetic agents. Dose adjustments of the antidiabetic agents may be needed. Altered blood glucose control, resulting in serious symptomatic hypoglycemia, has been reported in diabetic patients receiving antidiabetic agents in combination with direct acting antivirals, such as elbasvir.
Empagliflozin; Linagliptin; Metformin: (Moderate) Monitor blood glucose during concomitant sulfonylurea and metformin use; a sulfonylurea dose adjustment may be necessary. Concomitant use may cause an increased blood glucose-lowering effect with risk of hypoglycemia.
Empagliflozin; Metformin: (Moderate) Monitor blood glucose during concomitant sulfonylurea and metformin use; a sulfonylurea dose adjustment may be necessary. Concomitant use may cause an increased blood glucose-lowering effect with risk of hypoglycemia.
Enalapril, Enalaprilat: (Moderate) Monitor blood glucose during concomitant sulfonylurea and angiotensin-converting enzyme (ACE) inhibitor use. Concomitant use may cause an increased blood glucose-lowering effect with risk of hypoglycemia.
Enalapril; Felodipine: (Moderate) Monitor blood glucose during concomitant sulfonylurea and angiotensin-converting enzyme (ACE) inhibitor use. Concomitant use may cause an increased blood glucose-lowering effect with risk of hypoglycemia.
Enalapril; Hydrochlorothiazide, HCTZ: (Moderate) Monitor blood glucose during concomitant sulfonylurea and angiotensin-converting enzyme (ACE) inhibitor use. Concomitant use may cause an increased blood glucose-lowering effect with risk of hypoglycemia.
Ephedrine: (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.
Ephedrine; Guaifenesin: (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.
Epinephrine: (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.
Eprosartan: (Moderate) Monitor blood glucose during concomitant sulfonylurea and angiotensin receptor blocker use. Concomitant use may cause an increased blood glucose-lowering effect with risk of hypoglycemia.
Eprosartan; Hydrochlorothiazide, HCTZ: (Moderate) Monitor blood glucose during concomitant sulfonylurea and angiotensin receptor blocker use. Concomitant use may cause an increased blood glucose-lowering effect with risk of hypoglycemia.
Eravacycline: (Moderate) Use sulfonylureas and eravacycline together with caution; the risk of severe burns/photosensitivity may be additive. If concurrent use is necessary, closely monitor patients for signs or symptoms of skin toxicity. Prevention of photosensitivity includes adequate protection from sources of UV radiation and the use of protective clothing and sunscreens on exposed skin.
Ertugliflozin; Metformin: (Moderate) Monitor blood glucose during concomitant sulfonylurea and metformin use; a sulfonylurea dose adjustment may be necessary. Concomitant use may cause an increased blood glucose-lowering effect with risk of hypoglycemia.
Esmolol: (Moderate) Increased frequency of blood glucose monitoring may be required when a beta blocker is given with antidiabetic agents. Since beta blockers inhibit the release of catecholamines, these medications may hide symptoms of hypoglycemia such as tremor, tachycardia, and blood pressure changes. Other symptoms, like headache, dizziness, nervousness, mood changes, or hunger are not blunted. Beta-blockers also exert complex actions on the body's ability to regulate blood glucose. Some beta-blockers, particularly non-selective beta-blockers such as propranolol, have been noted to potentiate insulin-induced hypoglycemia and a delay in recovery of blood glucose to normal levels. Hyperglycemia has been reported as well and is possibly due to beta-2 receptor blockade in the beta cells of the pancreas. A selective beta-blocker may be preferred in patients with diabetes mellitus, if appropriate for the patient's condition. Selective beta-blockers, such as atenolol or metoprolol, do not appear to potentiate insulin-induced hypoglycemia. While beta-blockers may have negative effects on glycemic control, they reduce the risk of cardiovascular disease and stroke in patients with diabetes and their use should not be avoided in patients with compelling indications for beta-blocker therapy when no other contraindications are present.
Esterified Estrogens: (Minor) Patients receiving antidiabetic agents should be periodically monitored for changes in glycemic control when hormone therapy is instituted or discontinued. Estrogens can decrease the hypoglycemic effects of antidiabetic agents by impairing glucose tolerance. Changes in glucose

tolerance occur more commonly in patients receiving 50 mcg or more of ethinyl estradiol (or equivalent) per day in combined oral contraceptives (COCs), which are not commonly used in practice since the marketing of lower dose COCs, patches, injections and rings. The presence or absence of a concomitant progestin may influence the significance of any hormonal effect on glucose homeostasis.
Esterified Estrogens; Methyltestosterone: (Moderate) Changes in insulin sensitivity or glycemic control may occur in patients treated with androgens. In diabetic patients, the metabolic effects of androgens may decrease blood glucose and, therefore, may decrease antidiabetic agent dosage requirements. Monitor blood glucose and HbA1C when these drugs are used together. (Minor) Patients receiving antidiabetic agents should be periodically monitored for changes in glycemic control when hormone therapy is instituted or discontinued. Estrogens can decrease the hypoglycemic effects of antidiabetic agents by impairing glucose tolerance. Changes in glucose tolerance occur more commonly in patients receiving 50 mcg or more of ethinyl estradiol (or equivalent) per day in combined oral contraceptives (COCs), which are not commonly used in practice since the marketing of lower dose COCs, patches, injections and rings. The presence or absence of a concomitant progestin may influence the significance of any hormonal effect on glucose homeostasis.
Estradiol Cypionate; Medroxyprogesterone: (Minor) Patients receiving antidiabetic agents should be periodically monitored for changes in glycemic control when hormone therapy is instituted or discontinued. Estrogens can decrease the hypoglycemic effects of antidiabetic agents by impairing glucose tolerance. Changes in glucose tolerance occur more commonly in patients receiving 50 mcg or more of ethinyl estradiol (or equivalent) per day in combined oral contraceptives (COCs), which are not commonly used in practice since the marketing of lower dose COCs, patches, injections and rings. The presence or absence of a concomitant progestin may influence the significance of any hormonal effect on glucose homeostasis.
Estradiol: (Minor) Patients receiving antidiabetic agents should be periodically monitored for changes in glycemic control when hormone therapy is instituted or discontinued. Estrogens can decrease the hypoglycemic effects of antidiabetic agents by impairing glucose tolerance. Changes in glucose tolerance occur more commonly in patients receiving 50 mcg or more of ethinyl estradiol (or equivalent) per day in combined oral contraceptives (COCs), which are not commonly used in practice since the marketing of lower dose COCs, patches, injections and rings. The presence or absence of a concomitant progestin may influence the significance of any hormonal effect on glucose homeostasis.
Estradiol; Levonorgestrel: (Minor) Patients receiving antidiabetic agents should be periodically monitored for changes in glycemic control when hormone therapy is instituted or discontinued. Estrogens can decrease the hypoglycemic effects of antidiabetic agents by impairing glucose tolerance. Changes in glucose tolerance occur more commonly in patients receiving 50 mcg or more of ethinyl estradiol (or equivalent) per day in combined oral contraceptives (COCs), which are not commonly used in practice since the marketing of lower dose COCs, patches, injections and rings. The presence or absence of a concomitant progestin may influence the significance of any hormonal effect on glucose homeostasis.
Estradiol; Norethindrone: (Minor) Patients receiving antidiabetic agents should be periodically monitored for changes in glycemic control when hormone therapy is instituted or discontinued. Estrogens can decrease the hypoglycemic effects of antidiabetic agents by impairing glucose tolerance. Changes in glucose tolerance occur more commonly in patients receiving 50 mcg or more of ethinyl estradiol (or equivalent) per day in combined oral contraceptives (COCs), which are not commonly used in practice since the marketing of lower dose COCs, patches, injections and rings. The presence or absence of a concomitant progestin may influence the significance of any hormonal effect on glucose homeostasis.
Estradiol; Norgestimate: (Minor) Patients receiving antidiabetic agents should be periodically monitored for changes in glycemic control when hormone therapy is instituted or discontinued. Estrogens can decrease the hypoglycemic effects of antidiabetic agents by impairing glucose tolerance. Changes in glucose tolerance occur more commonly in patients receiving 50 mcg or more of ethinyl estradiol (or

equivalent) per day in combined oral contraceptives (COCs), which are not commonly used in practice since the marketing of lower dose COCs, patches, injections and rings. The presence or absence of a concomitant progestin may influence the significance of any hormonal effect on glucose homeostasis.
Estradiol; Progesterone: (Minor) Patients receiving antidiabetic agents should be periodically monitored for changes in glycemic control when hormone therapy is instituted or discontinued. Estrogens can decrease the hypoglycemic effects of antidiabetic agents by impairing glucose tolerance. Changes in glucose tolerance occur more commonly in patients receiving 50 mcg or more of ethinyl estradiol (or equivalent) per day in combined oral contraceptives (COCs), which are not commonly used in practice since the marketing of lower dose COCs, patches, injections and rings. The presence or absence of a concomitant progestin may influence the significance of any hormonal effect on glucose homeostasis.
Estramustine: (Minor) Estramustine is an estrogen-containing medication and may decrease glucose tolerance. Patients receiving antidiabetic agents should monitor their blood glucose levels frequently due to this potential pharmacodynamic interaction.
Estrogens: (Minor) Patients receiving antidiabetic agents should be periodically monitored for changes in glycemic control when hormone therapy is instituted or discontinued. Estrogens can decrease the hypoglycemic effects of antidiabetic agents by impairing glucose tolerance. Changes in glucose tolerance occur more commonly in patients receiving 50 mcg or more of ethinyl estradiol (or equivalent) per day in combined oral contraceptives (COCs), which are not commonly used in practice since the marketing of lower dose COCs, patches, injections and rings. The presence or absence of a concomitant progestin may influence the significance of any hormonal effect on glucose homeostasis.
Estropipate: (Minor) Patients receiving antidiabetic agents should be periodically monitored for changes in glycemic control when hormone therapy is instituted or discontinued. Estrogens can decrease the hypoglycemic effects of antidiabetic agents by impairing glucose tolerance. Changes in glucose tolerance occur more commonly in patients receiving 50 mcg or more of ethinyl estradiol (or equivalent) per day in combined oral contraceptives (COCs), which are not commonly used in practice since the marketing of lower dose COCs, patches, injections and rings. The presence or absence of a concomitant progestin may influence the significance of any hormonal effect on glucose homeostasis.
Ethanol: (Major) Patients should be advised to avoid or limit alcohol ingestion when treated with sulfonylureas. Alcohol ingestion increases hypoglycemic risk. In some patients, hypoglycemia can be prolonged. Patients should be educated regarding the signs, symptoms, and self-management of delayed hypoglycemia after drinking alcohol, especially when using sulfonylureas. The importance of glucose monitoring after drinking alcoholic beverages to reduce hypoglycemia risk should be emphasized.
Ethinyl Estradiol: (Minor) Patients receiving antidiabetic agents should be periodically monitored for changes in glycemic control when hormone therapy is instituted or discontinued. Estrogens can decrease the hypoglycemic effects of antidiabetic agents by impairing glucose tolerance. Changes in glucose tolerance occur more commonly in patients receiving 50 mcg or more of ethinyl estradiol (or equivalent) per day in combined oral contraceptives (COCs), which are not commonly used in practice since the marketing of lower dose COCs, patches, injections and rings. The presence or absence of a concomitant progestin may influence the significance of any hormonal effect on glucose homeostasis.
Ethinyl Estradiol; Levonorgestrel; Folic Acid; Levomefolate: (Minor) Patients receiving antidiabetic agents should be periodically monitored for changes in glycemic control when hormone therapy is instituted or discontinued. Estrogens can decrease the hypoglycemic effects of antidiabetic agents by impairing glucose tolerance. Changes in glucose tolerance occur more commonly in patients receiving 50 mcg or more of ethinyl estradiol (or equivalent) per day in combined oral contraceptives (COCs), which are not commonly used in practice since the marketing of lower dose COCs, patches, injections and rings. The presence or absence of a concomitant progestin may influence the significance of any hormonal effect on glucose homeostasis.
Ethinyl Estradiol; Norelgestromin: (Minor) Patients receiving antidiabetic agents should be periodically

monitored for changes in glycemic control when hormone therapy is instituted or discontinued. Estrogens can decrease the hypoglycemic effects of antidiabetic agents by impairing glucose tolerance. Changes in glucose tolerance occur more commonly in patients receiving 50 mcg or more of ethinyl estradiol (or equivalent) per day in combined oral contraceptives (COCs), which are not commonly used in practice since the marketing of lower dose COCs, patches, injections and rings. The presence or absence of a concomitant progestin may influence the significance of any hormonal effect on glucose homeostasis.
Ethinyl Estradiol; Norethindrone Acetate: (Minor) Patients receiving antidiabetic agents should be periodically monitored for changes in glycemic control when hormone therapy is instituted or discontinued. Estrogens can decrease the hypoglycemic effects of antidiabetic agents by impairing glucose tolerance. Changes in glucose tolerance occur more commonly in patients receiving 50 mcg or more of ethinyl estradiol (or equivalent) per day in combined oral contraceptives (COCs), which are not commonly used in practice since the marketing of lower dose COCs, patches, injections and rings. The presence or absence of a concomitant progestin may influence the significance of any hormonal effect on glucose homeostasis.
Ethinyl Estradiol; Norgestrel: (Minor) Patients receiving antidiabetic agents should be periodically monitored for changes in glycemic control when hormone therapy is instituted or discontinued. Estrogens can decrease the hypoglycemic effects of antidiabetic agents by impairing glucose tolerance. Changes in glucose tolerance occur more commonly in patients receiving 50 mcg or more of ethinyl estradiol (or equivalent) per day in combined oral contraceptives (COCs), which are not commonly used in practice since the marketing of lower dose COCs, patches, injections and rings. The presence or absence of a concomitant progestin may influence the significance of any hormonal effect on glucose homeostasis.
Ethotoin: (Minor) Phenytoin and other hydantoins have the potential to increase blood glucose and thus interact with antidiabetic agents pharmacodynamically. In addition, coadministration may result in decreased serum concentrations of chlorpropamide. Monitor blood glucose for changes in glycemic control. Dosage adjustments may be necessary in some patients.
Ethynodiol Diacetate; Ethinyl Estradiol: (Minor) Patients receiving antidiabetic agents should be periodically monitored for changes in glycemic control when hormone therapy is instituted or discontinued. Estrogens can decrease the hypoglycemic effects of antidiabetic agents by impairing glucose tolerance. Changes in glucose tolerance occur more commonly in patients receiving 50 mcg or more of ethinyl estradiol (or equivalent) per day in combined oral contraceptives (COCs), which are not commonly used in practice since the marketing of lower dose COCs, patches, injections and rings. The presence or absence of a concomitant progestin may influence the significance of any hormonal effect on glucose homeostasis.
Etonogestrel; Ethinyl Estradiol: (Minor) Patients receiving antidiabetic agents should be periodically monitored for changes in glycemic control when hormone therapy is instituted or discontinued. Estrogens can decrease the hypoglycemic effects of antidiabetic agents by impairing glucose tolerance. Changes in glucose tolerance occur more commonly in patients receiving 50 mcg or more of ethinyl estradiol (or equivalent) per day in combined oral contraceptives (COCs), which are not commonly used in practice since the marketing of lower dose COCs, patches, injections and rings. The presence or absence of a concomitant progestin may influence the significance of any hormonal effect on glucose homeostasis.
Exenatide: (Moderate) The risk of hypoglycemia is increased when exenatide is used in combination with insulins or insulin secretagogues such as the sulfonylureas. Although specific dose recommendations are not available, a lower dose of the insulin or secretagogue may be required to reduce the risk of hypoglycemia in this setting. Adequate blood glucose monitoring should be continued and followed.
Fenofibrate: (Moderate) Monitor blood glucose during concomitant sulfonylurea and fenofibrate use; a sulfonylurea dose adjustment may be necessary. Concomitant use may cause an increased blood glucose-lowering effect with risk of hypoglycemia.
Fenofibric Acid: (Moderate) Monitor blood glucose during concomitant sulfonylurea and fenofibric acid

use; a sulfonylurea dose adjustment may be necessary. Concomitant use may cause an increased blood glucose-lowering effect with risk of hypoglycemia.
Fexofenadine; Pseudoephedrine: (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.
Fluconazole: (Moderate) Fluconazole should be used cautiously with oral sulfonylureas because blood glucose response may be altered in diabetic patients. In some cases, dosage adjustment of the sulfonylurea may be necessary.
Fluocinolone; Hydroquinone; Tretinoin: (Moderate) A manufacturer of topical tretinoin states that tretinoin, ATRA should be administered with caution in patients who are also taking drugs known to be photosensitizers, such as sulfonylureas, as concomitant use may augment phototoxicity. Patients should take care and use proper techniques to limit sunlight and UV exposure of treated areas.
Fluoxetine: (Moderate) Monitor blood glucose during concomitant sulfonylurea and fluoxetine use; a sulfonylurea dose adjustment may be necessary. Concomitant use may cause an increased blood glucose-lowering effect with risk of hypoglycemia.
Fluoxymesterone: (Moderate) Changes in insulin sensitivity or glycemic control may occur in patients treated with androgens. In diabetic patients, the metabolic effects of androgens may decrease blood glucose and, therefore, may decrease antidiabetic agent dosage requirements. Monitor blood glucose and HbA1C when these drugs are used together.
Fosamprenavir: (Moderate) New onset diabetes mellitus, exacerbation of diabetes mellitus, and hyperglycemia due to insulin resistance have been reported with use of anti-retroviral protease inhibitors. A possible mechanism is impairment of beta-cell function. Onset averaged approximately 63 days after initiating protease inhibitor therapy, but has occurred as early as 4 days after beginning therapy. Diabetic ketoacidosis has occurred in some patients including patients who were not diabetic prior to protease inhibitor treatment. Patients on antidiabetic agents should be closely monitored for changes in glycemic control, specifically hyperglycemia, if protease inhibitor therapy is initiated.
Fosinopril: (Moderate) Monitor blood glucose during concomitant sulfonylurea and angiotensin-converting enzyme (ACE) inhibitor use. Concomitant use may cause an increased blood glucose-lowering effect with risk of hypoglycemia.
Fosinopril; Hydrochlorothiazide, HCTZ: (Moderate) Monitor blood glucose during concomitant sulfonylurea and angiotensin-converting enzyme (ACE) inhibitor use. Concomitant use may cause an increased blood glucose-lowering effect with risk of hypoglycemia.
Fosphenytoin: (Minor) Phenytoin and other hydantoins have the potential to increase blood glucose and thus interact with antidiabetic agents pharmacodynamically. In addition, coadministration may result in decreased serum concentrations of chlorpropamide. Monitor blood glucose for changes in glycemic control. Dosage adjustments may be necessary in some patients.
Furosemide: (Minor) Furosemide may cause hyperglycemia and glycosuria in patients with diabetes mellitus. This interference can lead to a loss of diabetic control, so diabetic patients should be monitored closely.
Garlic, Allium sativum: (Moderate) Patients receiving antidiabetic agents should use dietary supplements of Garlic, Allium sativum with caution. Constituents in garlic might have some antidiabetic activity, and may increase serum insulin levels and increase glycogen storage in the liver. Monitor blood glucose and glycemic control. Patients with diabetes should inform their health care professionals of their intent to

ingest garlic dietary supplements. Some patients may require adjustment to their hypoglycemic medications over time. One study stated that additional garlic supplementation (0.05 to 1.5 grams PO per day) contributed to improved blood glucose control in patients with type 2 diabetes mellitus within 1 to 2 weeks, and had positive effects on total cholesterol and high/low density lipoprotein regulation over time. It is unclear if hemoglobin A1C is improved or if improvements are sustained with continued treatment beyond 24 weeks. Other reviews suggest that garlic may provide modest improvements in blood lipids, but few studies demonstrate decreases in blood glucose in diabetic and non-diabetic patients. More controlled trials are needed to discern if garlic has an effect on blood glucose in patients with diabetes. When garlic is used in foods or as a seasoning, or at doses of 50 mg/day or less, it is unlikely that blood glucose levels are affected to any clinically significant degree.

Gemfibrozil: (Moderate) There is an increased risk for hypoglycemia when gemfibrozil is used with sulfonylureas. Dose reductions and increased frequency of glucose monitoring may be required. Gemfibrozil is a potent inhibitor of CYP2C9, which metabolizes many of the sulfonylureas. In addition, glyburide is a substrate of the OATP1B1 transporter and gemfibrozil inhibits OATP1B1. Due to the effects of gemfibrozil on sulfonylurea metabolic pathways, an increase in sulfonylurea exposure may occur. Fibric acid derivatives may also enhance the hypoglycemic effects of antidiabetic agents through increased insulin sensitivity and increased glucagon secretion.

Glecaprevir; Pibrentasvir: (Moderate) Closely monitor blood glucose levels if glecaprevir is administered with antidiabetic agents. Dose adjustments of the antidiabetic agents may be needed. Altered blood glucose control, resulting in serious symptomatic hypoglycemia, has been reported in diabetic patients receiving antidiabetic agents in combination with direct acting antivirals, such as glecaprevir. (Moderate) Closely monitor blood glucose levels if pibrentasvir is administered with antidiabetic agents. Dose adjustments of the antidiabetic agents may be needed. Altered blood glucose control, resulting in serious symptomatic hypoglycemia, has been reported in diabetic patients receiving antidiabetic agents in combination with direct acting antivirals, such as pibrentasvir.

Glimepiride; Rosiglitazone: (Major) A maximum dose of 8 mg/day of rosiglitazone is recommended when used in combination with sulfonylureas; the incidence of adverse effects including hypoglycemia is increased with larger doses. In one clinical study, rosiglitazone 4 or 8 mg/day was added to failed glimepiride plus metformin therapy. The incidence of hypoglycemia (blood glucose concentrations <= 50 mg/dl) was 18.6% in the 4 mg/day group compared with 28% in the 8 mg/day group. In addition, 4 or 8 mg/day of rosiglitazone has been added to failed glyburide plus metformin therapy. The incidence of hypoglycemia was higher in the rosiglitazone (average dose 7.4 mg/day)+glyburide+metformin group (22%) when compared to the glyburide+metformin group (3%). Patients should be instructed to monitor blood glucose concentrations more frequently. Dosage adjustments may be indicated.

Glipizide; Metformin: (Moderate) Monitor blood glucose during concomitant sulfonylurea and metformin use; a sulfonylurea dose adjustment may be necessary. Concomitant use may cause an increased blood glucose-lowering effect with risk of hypoglycemia.

Glyburide; Metformin: (Moderate) Monitor blood glucose during concomitant sulfonylurea and metformin use; a sulfonylurea dose adjustment may be necessary. Concomitant use may cause an increased blood glucose-lowering effect with risk of hypoglycemia.

Green Tea: (Moderate) Green tea catechins have been shown to decrease serum glucose concentrations in vitro. Patients with diabetes mellitus taking antidiabetic agents should be monitored closely for hypoglycemia if consuming green tea products.

Griseofulvin: (Moderate) Additive photosensitization may be seen with concurrent administration of sulfonylureas and other photosensitizing agents including griseofulvin. Prevention of photosensitivity includes adequate protection from sources of UV radiation (e.g., avoiding sun exposure and tanning booths) and the use of protective clothing and sunscreens on exposed skin.

Guaifenesin; Hydrocodone; Pseudoephedrine: (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.

Guaifenesin; Phenylephrine: (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.

Guaifenesin; Pseudoephedrine: (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.

Halobetasol; Tazarotene: (Moderate) The manufacturer states that tazarotene should be administered with caution in patients who are also taking drugs known to be photosensitizers, such as sulfonylureas, as concomitant use may augment phototoxicity. Patients should take care and use proper techniques to limit sunlight and UV exposure of treated areas.

Hydantoins: (Minor) Phenytoin and other hydantoins have the potential to increase blood glucose and thus interact with antidiabetic agents pharmacodynamically. In addition, coadministration may result in decreased serum concentrations of chlorpropamide. Monitor blood glucose for changes in glycemic control. Dosage adjustments may be necessary in some patients.

Hydrochlorothiazide, HCTZ; Moexipril: (Moderate) Monitor blood glucose during concomitant sulfonylurea and angiotensin-converting enzyme (ACE) inhibitor use. Concomitant use may cause an increased blood glucose-lowering effect with risk of hypoglycemia.

Hydrocodone; Phenylephrine: (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.

Hydrocodone; Potassium Guaiacolsulfonate; Pseudoephedrine: (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.
Hydrocodone; Pseudoephedrine: (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.
Hydroxychloroquine: (Moderate) Monitor blood glucose during concomitant sulfonylurea and hydroxychloroquine use; a sulfonylurea dose adjustment may be necessary. Concomitant use may cause an increased blood glucose-lowering effect with risk of hypoglycemia.
Hydroxyprogesterone: (Minor) Progestins, like hydroxyprogesterone, can impair glucose tolerance. Patients receiving antidiabetic agents should be closely monitored for signs indicating changes in diabetic control when therapy with progestins is instituted or discontinued.
Ibuprofen; Pseudoephedrine: (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.
Iloperidone: (Moderate) Atypical antipsychotic therapy may aggravate diabetes mellitus and cause metabolic changes such as hyperglycemia. Monitor patients on antidiabetic agents for worsening glycemic control. The atypical antipsychotics have been associated with metabolic changes, including hyperglycemia, diabetic ketoacidosis, hyperosmolar, hyperglycemic states, and diabetic coma. Aggravation of diabetes mellitus has been reported. Possible mechanisms include atypical antipsychotic-induced insulin resistance or direct beta-cell inhibition.
Indapamide: (Moderate) A potential pharmacodynamic interaction exists between indapamide and antidiabetic agents, like sulfonylureas. Indapamide can decrease insulin sensitivity thereby leading to glucose intolerance and hyperglycemia. Diuretic-induced hypokalemia may also lead to hyperglycemia.
Indinavir: (Moderate) New onset diabetes mellitus, exacerbation of diabetes mellitus, and hyperglycemia due to insulin resistance have been reported with use of anti-retroviral protease inhibitors. A possible mechanism is impairment of beta-cell function. Onset averaged approximately 63 days after initiating protease inhibitor therapy, but has occurred as early as 4 days after beginning therapy. Diabetic ketoacidosis has occurred in some patients including patients who were not diabetic prior to protease inhibitor treatment. Patients on antidiabetic agents should be closely monitored for changes in glycemic control, specifically hyperglycemia, if protease inhibitor therapy is initiated.
Insulin Degludec; Liraglutide: (Moderate) Consider reducing the sulfonylurea dose when initiating liraglutide to reduce the risk for hypoglycemia. Patients receiving liraglutide in combination with a sulfonylurea may have an increased risk of hypoglycemia, including severe hypoglycemia.
Insulin Glargine; Lixisenatide: (Moderate) The risk of hypoglycemia is increased when lixisenatide is used in combination with insulin secretagogues such as the sulfonylureas. Although specific dose recommendations are not available, a lower dose of the sulfonylurea may be required to reduce the risk of hypoglycemia in this setting. Adequate blood glucose monitoring should be continued and followed.
Irbesartan: (Moderate) Monitor blood glucose during concomitant sulfonylurea and angiotensin receptor

blocker use. Concomitant use may cause an increased blood glucose-lowering effect with risk of hypoglycemia.
Irbesartan; Hydrochlorothiazide, HCTZ: (Moderate) Monitor blood glucose during concomitant sulfonylurea and angiotensin receptor blocker use. Concomitant use may cause an increased blood glucose-lowering effect with risk of hypoglycemia.
Isocarboxazid: (Moderate) Monitor blood glucose during concomitant sulfonylurea and monoamine oxidase inhibitor (MAOI) use; a sulfonylurea dose adjustment may be necessary. Concomitant use may cause an increased blood glucose-lowering effect with risk of hypoglycemia.
Isoproterenol: (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.
Itraconazole: (Moderate) Itraconazole should be used cautiously with oral antidiabetic agents like sulfonylureas. The combination of itraconazole and oral antidiabetic agents has resulted in severe hypoglycemia. Blood glucose concentrations should be monitored and possible dose adjustments of hypoglycemics may need to be made.
Ketoconazole: (Moderate) Hypoglycemia, sometimes severe, has been reported when ketoconazole is coadministered with oral hypoglycemic agents. The most likely mechanism for this interaction is inhibition of the CYP450 metabolism of oral hypoglycemics by ketoconazole. Blood glucose concentrations should be monitored during concomitant treatment; patients should be aware of the symptoms of hypoglycemia. In some cases, dosage adjustment of the sulfonylurea may be necessary. There is no evidence that an interaction occurs between oral hypoglycemics and topical or vaginal azole antifungal preparations.
Labetalol: (Moderate) Increased frequency of blood glucose monitoring may be required when a beta blocker is given with antidiabetic agents. Since beta blockers inhibit the release of catecholamines, these medications may hide symptoms of hypoglycemia such as tremor, tachycardia, and blood pressure changes. Other symptoms, like headache, dizziness, nervousness, mood changes, or hunger are not blunted. Beta-blockers also exert complex actions on the body's ability to regulate blood glucose. Some beta-blockers, particularly non-selective beta-blockers such as propranolol, have been noted to potentiate insulin-induced hypoglycemia and a delay in recovery of blood glucose to normal levels. Hyperglycemia has been reported as well and is possibly due to beta-2 receptor blockade in the beta cells of the pancreas. A selective beta-blocker may be preferred in patients with diabetes mellitus, if appropriate for the patient's condition. Selective beta-blockers, such as atenolol or metoprolol, do not appear to potentiate insulin-induced hypoglycemia. While beta-blockers may have negative effects on glycemic control, they reduce the risk of cardiovascular disease and stroke in patients with diabetes and their use should not be avoided in patients with compelling indications for beta-blocker therapy when no other contraindications are present.
Lanreotide: (Moderate) Monitor blood glucose levels regularly in patients with diabetes, especially when lanreotide treatment is initiated or when the dose is altered. Adjust treatment with antidiabetic agents as clinically indicated. Lanreotide inhibits the secretion of insulin and glucagon. Patients treated with lanreotide may experience either hypoglycemia or hyperglycemia.
Lansoprazole; Amoxicillin; Clarithromycin: (Moderate) The concomitant use of clarithromycin and antidiabetic agents can result in significant hypoglycemia. Careful monitoring of blood glucose is recommended.
Ledipasvir; Sofosbuvir: (Moderate) Closely monitor blood glucose levels if ledipasvir is administered with

antidiabetic agents. Dose adjustments of the antidiabetic agent(s) may be needed. Altered blood glucose control, resulting in serious symptomatic hypoglycemia, has been reported in diabetic patients receiving antidiabetic agents in combination with direct acting antivirals, such as ledipasvir. (Moderate) Closely monitor blood glucose levels if sofosbuvir is administered with antidiabetic agents. Dose adjustments of the antidiabetic agents may be needed. Altered blood glucose control, resulting in serious symptomatic hypoglycemia, has been reported in diabetic patients receiving antidiabetic agents in combination with direct acting antivirals, such as sofosbuvir.

Lesinurad; Allopurinol: (Minor) Limited evidence suggests that concurrent allopurinol can interfere with chlorpropamide elimination. It is proposed that allopurinol interferes with renal tubular secretion of chlorpropamide. If allopurinol is added to chlorpropamide therapy, patients should be monitored for hypoglycemia.

Levobetaxolol: (Moderate) Increased frequency of blood glucose monitoring may be required when a beta blocker is given with antidiabetic agents. Since beta blockers inhibit the release of catecholamines, these medications may hide symptoms of hypoglycemia such as tremor, tachycardia, and blood pressure changes. Other symptoms, like headache, dizziness, nervousness, mood changes, or hunger are not blunted. Beta-blockers also exert complex actions on the body's ability to regulate blood glucose. Some beta-blockers, particularly non-selective beta-blockers such as propranolol, have been noted to potentiate insulin-induced hypoglycemia and a delay in recovery of blood glucose to normal levels. Hyperglycemia has been reported as well and is possibly due to beta-2 receptor blockade in the beta cells of the pancreas. A selective beta-blocker may be preferred in patients with diabetes mellitus, if appropriate for the patient's condition. Selective beta-blockers, such as atenolol or metoprolol, do not appear to potentiate insulin-induced hypoglycemia. While beta-blockers may have negative effects on glycemic control, they reduce the risk of cardiovascular disease and stroke in patients with diabetes and their use should not be avoided in patients with compelling indications for beta-blocker therapy when no other contraindications are present.

Levobunolol: (Moderate) Increased frequency of blood glucose monitoring may be required when a beta blocker is given with antidiabetic agents. Since beta blockers inhibit the release of catecholamines, these medications may hide symptoms of hypoglycemia such as tremor, tachycardia, and blood pressure changes. Other symptoms, like headache, dizziness, nervousness, mood changes, or hunger are not blunted. Beta-blockers also exert complex actions on the body's ability to regulate blood glucose. Some beta-blockers, particularly non-selective beta-blockers such as propranolol, have been noted to potentiate insulin-induced hypoglycemia and a delay in recovery of blood glucose to normal levels. Hyperglycemia has been reported as well and is possibly due to beta-2 receptor blockade in the beta cells of the pancreas. A selective beta-blocker may be preferred in patients with diabetes mellitus, if appropriate for the patient's condition. Selective beta-blockers, such as atenolol or metoprolol, do not appear to potentiate insulin-induced hypoglycemia. While beta-blockers may have negative effects on glycemic control, they reduce the risk of cardiovascular disease and stroke in patients with diabetes and their use should not be avoided in patients with compelling indications for beta-blocker therapy when no other contraindications are present.

Levoketoconazole: (Moderate) Hypoglycemia, sometimes severe, has been reported when ketoconazole is coadministered with oral hypoglycemic agents. The most likely mechanism for this interaction is inhibition of the CYP450 metabolism of oral hypoglycemics by ketoconazole. Blood glucose concentrations should be monitored during concomitant treatment; patients should be aware of the symptoms of hypoglycemia. In some cases, dosage adjustment of the sulfonylurea may be necessary. There is no evidence that an interaction occurs between oral hypoglycemics and topical or vaginal azole antifungal preparations.

Levonorgestrel; Ethinyl Estradiol: (Minor) Patients receiving antidiabetic agents should be periodically monitored for changes in glycemic control when hormone therapy is instituted or discontinued. Estrogens can decrease the hypoglycemic effects of antidiabetic agents by impairing glucose tolerance. Changes in

glucose tolerance occur more commonly in patients receiving 50 mcg or more of ethinyl estradiol (or equivalent) per day in combined oral contraceptives (COCs), which are not commonly used in practice since the marketing of lower dose COCs, patches, injections and rings. The presence or absence of a concomitant progestin may influence the significance of any hormonal effect on glucose homeostasis.
Levonorgestrel; Ethinyl Estradiol; Ferrous Bisglycinate: (Minor) Patients receiving antidiabetic agents should be periodically monitored for changes in glycemic control when hormone therapy is instituted or discontinued. Estrogens can decrease the hypoglycemic effects of antidiabetic agents by impairing glucose tolerance. Changes in glucose tolerance occur more commonly in patients receiving 50 mcg or more of ethinyl estradiol (or equivalent) per day in combined oral contraceptives (COCs), which are not commonly used in practice since the marketing of lower dose COCs, patches, injections and rings. The presence or absence of a concomitant progestin may influence the significance of any hormonal effect on glucose homeostasis.
Lidocaine; Epinephrine: (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.
Linagliptin; Metformin: (Moderate) Monitor blood glucose during concomitant sulfonylurea and metformin use; a sulfonylurea dose adjustment may be necessary. Concomitant use may cause an increased blood glucose-lowering effect with risk of hypoglycemia.
Linezolid: (Moderate) Hypoglycemia, including symptomatic episodes, has been noted in post-marketing reports with linezolid in patients with diabetes mellitus receiving therapy with antidiabetic agents, such as insulin and oral hypoglycemic agents. Diabetic patients should be monitored for potential hypoglycemic reactions while on linezolid. If hypoglycemia occurs, discontinue or decrease the dose of the antidiabetic agent or discontinue the linezolid therapy. Linezolid is a reversible, nonselective MAO inhibitor and other MAO inhibitors have been associated with hypoglycemic episodes in diabetic patients receiving insulin or oral hypoglycemic agents.
Liraglutide: (Moderate) Consider reducing the sulfonylurea dose when initiating liraglutide to reduce the risk for hypoglycemia. Patients receiving liraglutide in combination with a sulfonylurea may have an increased risk of hypoglycemia, including severe hypoglycemia.
Lisdexamfetamine: (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.
Lisinopril: (Moderate) Monitor blood glucose during concomitant sulfonylurea and angiotensin-converting enzyme (ACE) inhibitor use. Concomitant use may cause an increased blood glucose-lowering effect with risk of hypoglycemia.
Lisinopril; Hydrochlorothiazide, HCTZ: (Moderate) Monitor blood glucose during concomitant sulfonylurea and angiotensin-converting enzyme (ACE) inhibitor use. Concomitant use may cause an increased blood glucose-lowering effect with risk of hypoglycemia.
Lithium: (Moderate) Lithium may cause variable effects on glycemic control when used in patients

receiving antidiabetic agents. Monitor blood glucose concentrations closely if lithium is coadministered with antidiabetic agents. Dosage adjustments of antidiabetic agents may be necessary.
Lixisenatide: (Moderate) The risk of hypoglycemia is increased when lixisenatide is used in combination with insulin secretagogues such as the sulfonylureas. Although specific dose recommendations are not available, a lower dose of the sulfonylurea may be required to reduce the risk of hypoglycemia in this setting. Adequate blood glucose monitoring should be continued and followed.
Lonapegsomatropin: (Moderate) Patients with diabetes mellitus should be monitored closely during somatropin (recombinant rhGH) therapy. Antidiabetic drugs (e.g., insulin or oral agents) may require adjustment when somatropin therapy is instituted in these patients. Growth hormones, such as somatropin, may decrease insulin sensitivity, leading to glucose intolerance and loss of blood glucose control. Therefore, glucose levels should be monitored periodically in all patients treated with somatropin, especially in those with risk factors for diabetes mellitus.
Lopinavir; Ritonavir: (Moderate) New onset diabetes mellitus, exacerbation of diabetes mellitus, and hyperglycemia due to insulin resistance have been reported with use of anti-retroviral protease inhibitors. A possible mechanism is impairment of beta-cell function. Onset averaged approximately 63 days after initiating protease inhibitor therapy, but has occurred as early as 4 days after beginning therapy. Diabetic ketoacidosis has occurred in some patients including patients who were not diabetic prior to protease inhibitor treatment. Patients on antidiabetic agents should be closely monitored for changes in glycemic control, specifically hyperglycemia, if protease inhibitor therapy is initiated.
Loratadine; Pseudoephedrine: (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.
Lorcaserin: (Moderate) In general, weight reduction may increase the risk of hypoglycemia in patients with type 2 diabetes mellitus treated with antidiabetic agents, such as insulin and/or insulin secretagogues (e.g., sulfonylureas). In clinical trials, lorcaserin use was associated with reports of hypoglycemia. Blood glucose monitoring is warranted in patients with type 2 diabetes prior to starting and during lorcaserin treatment. Dosage adjustments of anti-diabetic medications should be considered. If a patient develops hypoglycemia during treatment, adjust anti-diabetic drug regimen accordingly. Of note, lorcaserin has not been studied in combination with insulin.
Losartan: (Moderate) Monitor blood glucose during concomitant sulfonylurea and angiotensin receptor blocker use. Concomitant use may cause an increased blood glucose-lowering effect with risk of hypoglycemia.
Losartan; Hydrochlorothiazide, HCTZ: (Moderate) Monitor blood glucose during concomitant sulfonylurea and angiotensin receptor blocker use. Concomitant use may cause an increased blood glucose-lowering effect with risk of hypoglycemia.
Lovastatin; Niacin: (Moderate) Niacin (nicotinic acid) interferes with glucose metabolism and can result in hyperglycemia. Changes in glycemic control can usually be corrected through modification of hypoglycemic therapy. Monitor patients taking antidiabetic agents for changes in glycemic control if niacin (nicotinic acid) is added or deleted to the medication regimen. Dosage adjustments may be necessary.
Lumacaftor; Ivacaftor: (Moderate) Lumacaftor; ivacaftor may reduce the efficacy of chlorpropamide by decreasing its systemic exposure. If used together, monitor blood glucose concentrations closely; a chlorpropamide dosage adjustment may be required to obtain the desired therapeutic effect.

Chlorpropamide is a CYP2C9 substrate; in vitro studies suggest lumacaftor; ivacaftor has the potential to induce and inhibit CYP2C9.
Lumacaftor; Ivacaftor: (Moderate) Lumacaftor; ivacaftor may reduce the efficacy of chlorpropamide by decreasing its systemic exposure. If used together, monitor blood glucose concentrations closely; a chlorpropamide dosage adjustment may be required to obtain the desired therapeutic effect.
Chlorpropamide is a CYP2C9 substrate; in vitro studies suggest lumacaftor; ivacaftor has the potential to induce and inhibit CYP2C9.
Lumateperone: (Moderate) Atypical antipsychotic therapy may aggravate diabetes mellitus and cause metabolic changes such as hyperglycemia. Monitor patients on antidiabetic agents for worsening glycemic control. The atypical antipsychotics have been associated with metabolic changes, including hyperglycemia, diabetic ketoacidosis, hyperosmolar, hyperglycemic states, and diabetic coma. Aggravation of diabetes mellitus has been reported. Possible mechanisms include atypical antipsychotic-induced insulin resistance or direct beta-cell inhibition.
Lurasidone: (Moderate) Atypical antipsychotic therapy may aggravate diabetes mellitus and cause metabolic changes such as hyperglycemia. Monitor patients on antidiabetic agents for worsening glycemic control. The atypical antipsychotics have been associated with metabolic changes, including hyperglycemia, diabetic ketoacidosis, hyperosmolar, hyperglycemic states, and diabetic coma. Aggravation of diabetes mellitus has been reported. Possible mechanisms include atypical antipsychotic-induced insulin resistance or direct beta-cell inhibition.
Magnesium Salicylate: (Moderate) If salicylates and sulfonylureas are to be administered together, patients should be monitored for changes in glycemic control. Salicylates, by inhibiting prostaglandin E2 synthesis, can indirectly increase insulin secretion. Thus, salicylates can decrease blood sugar and may potentiate the effects of other antidiabetic agents. This mechanism may explain how salicylates can potentiate the clinical effects of sulfonylureas; however, displacement of sulfonylureas from protein binding sites has also been reported. In large doses, salicylates uncouple oxidative phosphorylation, deplete hepatic and muscle glycogen, and cause hyperglycemia and glycosuria.
Mecasermin rinfabate: (Moderate) Use caution in combining mecasermin, recombinant, rh-IGF-1 or mecasermin rinfabate (rh-IGF-1/rh-IGFBP-3) with antidiabetic agents. Patients should be advised to eat within 20 minutes of mecasermin administration. Glucose monitoring is important when initializing or adjusting mecasermin therapies, when adjusting concomitant antidiabetic therapy, and in the event of hypoglycemic symptoms. An increased risk for hypoglycemia is possible. The hypoglycemic effect induced by IGF-1 activity may be exacerbated. The amino acid sequence of mecasermin (rh-IGF-1) is approximately 50 percent homologous to insulin and cross binding with either receptor is possible. Treatment with mecasermin has been shown to improve insulin sensitivity and to improve glycemic control in patients with either Type 1 or Type 2 diabetes mellitus when used alone or in conjunction with insulins.
Mecasermin, Recombinant, rh-IGF-1: (Moderate) Use caution in combining mecasermin, recombinant, rh-IGF-1 or mecasermin rinfabate (rh-IGF-1/rh-IGFBP-3) with antidiabetic agents. Patients should be advised to eat within 20 minutes of mecasermin administration. Glucose monitoring is important when initializing or adjusting mecasermin therapies, when adjusting concomitant antidiabetic therapy, and in the event of hypoglycemic symptoms. An increased risk for hypoglycemia is possible. The hypoglycemic effect induced by IGF-1 activity may be exacerbated. The amino acid sequence of mecasermin (rh-IGF-1) is approximately 50 percent homologous to insulin and cross binding with either receptor is possible. Treatment with mecasermin has been shown to improve insulin sensitivity and to improve glycemic control in patients with either Type 1 or Type 2 diabetes mellitus when used alone or in conjunction with insulins.
Mepivacaine; Levonordefrin: (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.
Mequinol; Tretinoin: (Moderate) A manufacturer of topical tretinoin states that tretinoin, ATRA should be administered with caution in patients who are also taking drugs known to be photosensitizers, such as sulfonylureas, as concomitant use may augment phototoxicity. Patients should take care and use proper techniques to limit sunlight and UV exposure of treated areas.
Mestranol; Norethindrone: (Minor) Patients receiving antidiabetic agents should be periodically monitored for changes in glycemic control when hormone therapy is instituted or discontinued. Estrogens can decrease the hypoglycemic effects of antidiabetic agents by impairing glucose tolerance. Changes in glucose tolerance occur more commonly in patients receiving 50 mcg or more of ethinyl estradiol (or equivalent) per day in combined oral contraceptives (COCs), which are not commonly used in practice since the marketing of lower dose COCs, patches, injections and rings. The presence or absence of a concomitant progestin may influence the significance of any hormonal effect on glucose homeostasis.
Metformin: (Moderate) Monitor blood glucose during concomitant sulfonylurea and metformin use; a sulfonylurea dose adjustment may be necessary. Concomitant use may cause an increased blood glucose-lowering effect with risk of hypoglycemia.
Metformin; Repaglinide: (Moderate) Monitor blood glucose during concomitant sulfonylurea and metformin use; a sulfonylurea dose adjustment may be necessary. Concomitant use may cause an increased blood glucose-lowering effect with risk of hypoglycemia.
Metformin; Rosiglitazone: (Major) A maximum dose of 8 mg/day of rosiglitazone is recommended when used in combination with sulfonylureas; the incidence of adverse effects including hypoglycemia is increased with larger doses. In one clinical study, rosiglitazone 4 or 8 mg/day was added to failed glimepiride plus metformin therapy. The incidence of hypoglycemia (blood glucose concentrations <= 50 mg/dl) was 18.6% in the 4 mg/day group compared with 28% in the 8 mg/day group. In addition, 4 or 8 mg/day of rosiglitazone has been added to failed glyburide plus metformin therapy. The incidence of hypoglycemia was higher in the rosiglitazone (average dose 7.4 mg/day)+glyburide+metformin group (22%) when compared to the glyburide+metformin group (3%). Patients should be instructed to monitor blood glucose concentrations more frequently. Dosage adjustments may be indicated. (Moderate) Monitor blood glucose during concomitant sulfonylurea and metformin use; a sulfonylurea dose adjustment may be necessary. Concomitant use may cause an increased blood glucose-lowering effect with risk of hypoglycemia.
Metformin; Saxagliptin: (Moderate) A lower sulfonylurea dose may be required when used in combination with saxagliptin to minimize the risk of hypoglycemia. When saxagliptin was used in combination with a sulfonylurea, the incidence of hypoglycemia was increased compared to a placebo used in combination with a sulfonylurea. (Moderate) Monitor blood glucose during concomitant sulfonylurea and metformin use; a sulfonylurea dose adjustment may be necessary. Concomitant use may cause an increased blood glucose-lowering effect with risk of hypoglycemia.
Metformin; Sitagliptin: (Moderate) Monitor blood glucose during concomitant sulfonylurea and metformin use; a sulfonylurea dose adjustment may be necessary. Concomitant use may cause an increased blood glucose-lowering effect with risk of hypoglycemia.
Methamphetamine: (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.
Methotrexate: (Major) Avoid concomitant use of methotrexate and sulfonylureas due to the risk of severe methotrexate-related adverse reactions. If concomitant use is unavoidable, closely monitor for adverse reactions. Methotrexate is approximately 50% protein bound; sulfonylureas are highly protein-bound. Coadministration may displace methotrexate from its protein binding sites, increasing methotrexate plasma concentrations.
Methoxsalen: (Moderate) Additive photosensitization may be seen with concurrent administration of sulfonylureas and other photosensitizing agents.
Methylphenidate: (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.
Methyltestosterone: (Moderate) Changes in insulin sensitivity or glycemic control may occur in patients treated with androgens. In diabetic patients, the metabolic effects of androgens may decrease blood glucose and, therefore, may decrease antidiabetic agent dosage requirements. Monitor blood glucose and HbA1C when these drugs are used together.
Metoprolol: (Moderate) Increased frequency of blood glucose monitoring may be required when a beta blocker is given with antidiabetic agents. Since beta blockers inhibit the release of catecholamines, these medications may hide symptoms of hypoglycemia such as tremor, tachycardia, and blood pressure changes. Other symptoms, like headache, dizziness, nervousness, mood changes, or hunger are not blunted. Beta-blockers also exert complex actions on the body's ability to regulate blood glucose. Some beta-blockers, particularly non-selective beta-blockers such as propranolol, have been noted to potentiate insulin-induced hypoglycemia and a delay in recovery of blood glucose to normal levels. Hyperglycemia has been reported as well and is possibly due to beta-2 receptor blockade in the beta cells of the pancreas. A selective beta-blocker may be preferred in patients with diabetes mellitus, if appropriate for the patient's condition. Selective beta-blockers, such as atenolol or metoprolol, do not appear to potentiate insulin-induced hypoglycemia. While beta-blockers may have negative effects on glycemic control, they reduce the risk of cardiovascular disease and stroke in patients with diabetes and their use should not be avoided in patients with compelling indications for beta-blocker therapy when no other contraindications are present.
Metoprolol; Hydrochlorothiazide, HCTZ: (Moderate) Increased frequency of blood glucose monitoring may be required when a beta blocker is given with antidiabetic agents. Since beta blockers inhibit the release of catecholamines, these medications may hide symptoms of hypoglycemia such as tremor, tachycardia, and blood pressure changes. Other symptoms, like headache, dizziness, nervousness, mood changes, or hunger are not blunted. Beta-blockers also exert complex actions on the body's ability to regulate blood glucose. Some beta-blockers, particularly non-selective beta-blockers such as propranolol, have been noted to potentiate insulin-induced hypoglycemia and a delay in recovery of blood glucose to normal levels. Hyperglycemia has been reported as well and is possibly due to beta-2 receptor blockade in the beta cells of the pancreas. A selective beta-blocker may be preferred in patients with diabetes mellitus, if appropriate for the patient's condition. Selective beta-blockers, such as atenolol or metoprolol, do not appear to potentiate insulin-induced hypoglycemia. While beta-blockers may have negative effects on

glycemic control, they reduce the risk of cardiovascular disease and stroke in patients with diabetes and their use should not be avoided in patients with compelling indications for beta-blocker therapy when no other contraindications are present.
Metreleptin: (Moderate) Use caution when administering metreleptin to patients treated with concomitant insulins or insulin secretagogue therapy (i.e., sulfonylureas, nateglinide, repaglinide). In clinical evaluation of metreleptin, hypoglycemia occurred in 13% of patients with generalized lipodystrophy. Most reported cases occurred with concomitant insulin use, with or without oral antihyperglycemic agents. Closely monitor blood glucose in patients on concomitant insulin or insulin secretagogue therapy. Dosage adjustments to their antihyperglycemic medications may be necessary.
Metyrapone: (Moderate) In patients taking insulin or other antidiabetic agents, the signs and symptoms of acute metyrapone toxicity (e.g., symptoms of acute adrenal insufficiency) may be aggravated or modified.
Miconazole: (Moderate) Hypoglycemia, sometimes severe, has been reported when systemic azole antifungals are coadministered with sulfonylureas. No formal drug interaction studies have been performed with buccal miconazole. Miconazole is a known inhibitor of CYP2C9. Although the systemic absorption of miconazole following buccal administration is minimal and plasma concentrations are substantially lower than when miconazole is given intravenously, the potential for interaction with drugs metabolized through CYP2C9 (such as the sulfonylureas) cannot be ruled out.
Midodrine: (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: (Moderate) Additive photosensitization may be seen with concurrent administration of sulfonylureas and other photosensitizing agents including tetracyclines. Prevention of photosensitivity includes adequate protection from sources of UV radiation (e.g., avoiding sun exposure and tanning booths) and the use of protective clothing and sunscreens on exposed skin.
Moexipril: (Moderate) Monitor blood glucose during concomitant sulfonylurea and angiotensin-converting enzyme (ACE) inhibitor use. Concomitant use may cause an increased blood glucose-lowering effect with risk of hypoglycemia.
Monoamine oxidase inhibitors: (Moderate) Monitor blood glucose during concomitant sulfonylurea and monoamine oxidase inhibitor (MAOI) use; a sulfonylurea dose adjustment may be necessary. Concomitant use may cause an increased blood glucose-lowering effect with risk of hypoglycemia.
Nadolol: (Moderate) Increased frequency of blood glucose monitoring may be required when a beta blocker is given with antidiabetic agents. Since beta blockers inhibit the release of catecholamines, these medications may hide symptoms of hypoglycemia such as tremor, tachycardia, and blood pressure changes. Other symptoms, like headache, dizziness, nervousness, mood changes, or hunger are not blunted. Beta-blockers also exert complex actions on the body's ability to regulate blood glucose. Some beta-blockers, particularly non-selective beta-blockers such as propranolol, have been noted to potentiate insulin-induced hypoglycemia and a delay in recovery of blood glucose to normal levels. Hyperglycemia has been reported as well and is possibly due to beta-2 receptor blockade in the beta cells of the pancreas. A selective beta-blocker may be preferred in patients with diabetes mellitus, if appropriate for the patient's condition. Selective beta-blockers, such as atenolol or metoprolol, do not appear to potentiate insulin-induced hypoglycemia. While beta-blockers may have negative effects on glycemic control, they reduce the risk of cardiovascular disease and stroke in patients with diabetes and their use should not be avoided in patients with compelling indications for beta-blocker therapy when no other contraindications are

present.
Nandrolone Decanoate: (Moderate) Changes in insulin sensitivity or glycemic control may occur in patients treated with androgens. In diabetic patients, the metabolic effects of androgens may decrease blood glucose and, therefore, may decrease antidiabetic agent dosage requirements. Monitor blood glucose and HbA1C when these drugs are used together.
Naproxen; Pseudoephedrine: (Moderate) Sympathomimetic agents and adrenergic agonists tend to increase blood glucose concentrations when administered systemically. Monitor for loss of glycemic control when pseudoephedrine, phenylephrine, and other sympathomimetics are administered to patients taking antidiabetic agents. Epinephrine and other sympathomimetics, through stimulation of alpha- and beta-receptors, increase hepatic glucose production and glycogenolysis and inhibit insulin secretion. Also, adrenergic medications may decrease glucose uptake by muscle cells. For treatment of cold symptoms, nasal decongestants may be preferable for short term, limited use (1 to 3 days) as an alternative to systemic decongestants in patients taking medications for diabetes.
Nebivolol: (Moderate) Increased frequency of blood glucose monitoring may be required when a beta blocker is given with antidiabetic agents. Since beta blockers inhibit the release of catecholamines, these medications may hide symptoms of hypoglycemia such as tremor, tachycardia, and blood pressure changes. Other symptoms, like headache, dizziness, nervousness, mood changes, or hunger are not blunted. Beta-blockers also exert complex actions on the body's ability to regulate blood glucose. Some beta-blockers, particularly non-selective beta-blockers such as propranolol, have been noted to potentiate insulin-induced hypoglycemia and a delay in recovery of blood glucose to normal levels. Hyperglycemia has been reported as well and is possibly due to beta-2 receptor blockade in the beta cells of the pancreas. A selective beta-blocker may be preferred in patients with diabetes mellitus, if appropriate for the patient's condition. Selective beta-blockers, such as atenolol or metoprolol, do not appear to potentiate insulin-induced hypoglycemia. While beta-blockers may have negative effects on glycemic control, they reduce the risk of cardiovascular disease and stroke in patients with diabetes and their use should not be avoided in patients with compelling indications for beta-blocker therapy when no other contraindications are present.
Nebivolol; Valsartan: (Moderate) Increased frequency of blood glucose monitoring may be required when a beta blocker is given with antidiabetic agents. Since beta blockers inhibit the release of catecholamines, these medications may hide symptoms of hypoglycemia such as tremor, tachycardia, and blood pressure changes. Other symptoms, like headache, dizziness, nervousness, mood changes, or hunger are not blunted. Beta-blockers also exert complex actions on the body's ability to regulate blood glucose. Some beta-blockers, particularly non-selective beta-blockers such as propranolol, have been noted to potentiate insulin-induced hypoglycemia and a delay in recovery of blood glucose to normal levels. Hyperglycemia has been reported as well and is possibly due to beta-2 receptor blockade in the beta cells of the pancreas. A selective beta-blocker may be preferred in patients with diabetes mellitus, if appropriate for the patient's condition. Selective beta-blockers, such as atenolol or metoprolol, do not appear to potentiate insulin-induced hypoglycemia. While beta-blockers may have negative effects on glycemic control, they reduce the risk of cardiovascular disease and stroke in patients with diabetes and their use should not be avoided in patients with compelling indications for beta-blocker therapy when no other contraindications are present. (Moderate) Monitor blood glucose during concomitant sulfonylurea and angiotensin receptor blocker use. Concomitant use may cause an increased blood glucose-lowering effect with risk of hypoglycemia.
Nelfinavir: (Moderate) New onset diabetes mellitus, exacerbation of diabetes mellitus, and hyperglycemia due to insulin resistance have been reported with use of anti-retroviral protease inhibitors. A possible mechanism is impairment of beta-cell function. Onset averaged approximately 63 days after initiating protease inhibitor therapy, but has occurred as early as 4 days after beginning therapy. Diabetic ketoacidosis has occurred in some patients including patients who were not diabetic prior to protease

inhibitor treatment. Patients on antidiabetic agents should be closely monitored for changes in glycemic control, specifically hyperglycemia, if protease inhibitor therapy is initiated.
Niacin, Niacinamide: (Moderate) Niacin (nicotinic acid) interferes with glucose metabolism and can result in hyperglycemia. Changes in glycemic control can usually be corrected through modification of hypoglycemic therapy. Monitor patients taking antidiabetic agents for changes in glycemic control if niacin (nicotinic acid) is added or deleted to the medication regimen. Dosage adjustments may be necessary.
Niacin; Simvastatin: (Moderate) Niacin (nicotinic acid) interferes with glucose metabolism and can result in hyperglycemia. Changes in glycemic control can usually be corrected through modification of hypoglycemic therapy. Monitor patients taking antidiabetic agents for changes in glycemic control if niacin (nicotinic acid) is added or deleted to the medication regimen. Dosage adjustments may be necessary.
Nicotine: (Minor) Nicotine may increase plasma glucose. The cessation of nicotine therapy may result in a decrease in blood glucose. Blood glucose concentrations should be monitored more closely whenever a change in nicotine intake occurs; dosage adjustments in antidiabetic agents may be needed.
Nirmatrelvir; Ritonavir: (Moderate) New onset diabetes mellitus, exacerbation of diabetes mellitus, and hyperglycemia due to insulin resistance have been reported with use of anti-retroviral protease inhibitors. A possible mechanism is impairment of beta-cell function. Onset averaged approximately 63 days after initiating protease inhibitor therapy, but has occurred as early as 4 days after beginning therapy. Diabetic ketoacidosis has occurred in some patients including patients who were not diabetic prior to protease inhibitor treatment. Patients on antidiabetic agents should be closely monitored for changes in glycemic control, specifically hyperglycemia, if protease inhibitor therapy is initiated.
Nitazoxanide: (Moderate) The active metabolite of nitazoxanide, tizoxanide, is highly bound to plasma proteins. Caution should be exercised when administering nitazoxanide concurrently with other highly plasma protein-bound drugs with narrow therapeutic indices because competition for binding sites may occur.
Nonsteroidal antiinflammatory drugs: (Moderate) NSAIDs may enhance hypoglycemia in diabetic patients via inhibition of prostaglandin synthesis, which indirectly increases insulin secretion. If NSAIDs are administered or discontinued in patients receiving oral antidiabetic agents, patients should be monitored for hypoglycemia or loss of blood glucose control. No clinically significant interaction between sulindac at daily doses of 400 mg and oral hypoglycemic agents has been observed. Sulindac, its sulfide metabolite, and sulfonylureas are highly bound to protein. Sulindac could displace the sulfonylureas, altering hypoglycemic activity. Careful patient monitoring is recommended to ensure that no change in their diabetes medicine dosage is required. A sulfonylurea dose adjustment may be needed, especially if sulindac doses greater than 400 mg daily are used or if the drug combination is used in patients with renal impairment or other metabolic defects that might increase sulindac blood concentrations.
Norepinephrine: (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.
Norethindrone Acetate; Ethinyl Estradiol; Ferrous fumarate: (Minor) Patients receiving antidiabetic agents should be periodically monitored for changes in glycemic control when hormone therapy is instituted or discontinued. Estrogens can decrease the hypoglycemic effects of antidiabetic agents by impairing glucose tolerance. Changes in glucose tolerance occur more commonly in patients receiving 50 mcg or more of

ethinyl estradiol (or equivalent) per day in combined oral contraceptives (COCs), which are not commonly used in practice since the marketing of lower dose COCs, patches, injections and rings. The presence or absence of a concomitant progestin may influence the significance of any hormonal effect on glucose homeostasis.
Norethindrone; Ethinyl Estradiol: (Minor) Patients receiving antidiabetic agents should be periodically monitored for changes in glycemic control when hormone therapy is instituted or discontinued. Estrogens can decrease the hypoglycemic effects of antidiabetic agents by impairing glucose tolerance. Changes in glucose tolerance occur more commonly in patients receiving 50 mcg or more of ethinyl estradiol (or equivalent) per day in combined oral contraceptives (COCs), which are not commonly used in practice since the marketing of lower dose COCs, patches, injections and rings. The presence or absence of a concomitant progestin may influence the significance of any hormonal effect on glucose homeostasis.
Norethindrone; Ethinyl Estradiol; Ferrous fumarate: (Minor) Patients receiving antidiabetic agents should be periodically monitored for changes in glycemic control when hormone therapy is instituted or discontinued. Estrogens can decrease the hypoglycemic effects of antidiabetic agents by impairing glucose tolerance. Changes in glucose tolerance occur more commonly in patients receiving 50 mcg or more of ethinyl estradiol (or equivalent) per day in combined oral contraceptives (COCs), which are not commonly used in practice since the marketing of lower dose COCs, patches, injections and rings. The presence or absence of a concomitant progestin may influence the significance of any hormonal effect on glucose homeostasis.
Norgestimate; Ethinyl Estradiol: (Minor) Patients receiving antidiabetic agents should be periodically monitored for changes in glycemic control when hormone therapy is instituted or discontinued. Estrogens can decrease the hypoglycemic effects of antidiabetic agents by impairing glucose tolerance. Changes in glucose tolerance occur more commonly in patients receiving 50 mcg or more of ethinyl estradiol (or equivalent) per day in combined oral contraceptives (COCs), which are not commonly used in practice since the marketing of lower dose COCs, patches, injections and rings. The presence or absence of a concomitant progestin may influence the significance of any hormonal effect on glucose homeostasis.
Octreotide: (Moderate) Monitor patients receiving octreotide concomitantly with insulin or other antidiabetic agents for changes in glycemic control and adjust doses of these medications accordingly. Octreotide alters the balance between the counter-regulatory hormones of insulin, glucagon, and growth hormone, which may result in hypoglycemia or hyperglycemia. The hypoglycemia or hyperglycemia which occurs during octreotide acetate therapy is usually mild but may result in overt diabetes mellitus or necessitate dose changes in insulin or other hypoglycemic agents. In patients with concomitant type1 diabetes mellitus, octreotide is likely to affect glucose regulation, and insulin requirements may be reduced. Symptomatic hypoglycemia, which may be severe, has been reported in type 1 diabetic patients. In Type 2 diabetes patients with partially intact insulin reserves, octreotide administration may result in decreases in plasma insulin levels and hyperglycemia.
Olanzapine: (Moderate) Atypical antipsychotic therapy may aggravate diabetes mellitus and cause metabolic changes such as hyperglycemia. Monitor patients on antidiabetic agents for worsening glycemic control. The atypical antipsychotics have been associated with metabolic changes, including hyperglycemia, diabetic ketoacidosis, hyperosmolar, hyperglycemic states, and diabetic coma. Aggravation of diabetes mellitus has been reported. Possible mechanisms include atypical antipsychotic-induced insulin resistance or direct beta-cell inhibition.
Olanzapine; Fluoxetine: (Moderate) Atypical antipsychotic therapy may aggravate diabetes mellitus and cause metabolic changes such as hyperglycemia. Monitor patients on antidiabetic agents for worsening glycemic control. The atypical antipsychotics have been associated with metabolic changes, including hyperglycemia, diabetic ketoacidosis, hyperosmolar, hyperglycemic states, and diabetic coma. Aggravation of diabetes mellitus has been reported. Possible mechanisms include atypical antipsychotic-induced insulin resistance or direct beta-cell inhibition. (Moderate) Monitor blood glucose during

concomitant sulfonylurea and fluoxetine use; a sulfonylurea dose adjustment may be necessary. Concomitant use may cause an increased blood glucose-lowering effect with risk of hypoglycemia.
Olanzapine; Samidorphan: (Moderate) Atypical antipsychotic therapy may aggravate diabetes mellitus and cause metabolic changes such as hyperglycemia. Monitor patients on antidiabetic agents for worsening glycemic control. The atypical antipsychotics have been associated with metabolic changes, including hyperglycemia, diabetic ketoacidosis, hyperosmolar, hyperglycemic states, and diabetic coma. Aggravation of diabetes mellitus has been reported. Possible mechanisms include atypical antipsychotic-induced insulin resistance or direct beta-cell inhibition.
Olmesartan: (Moderate) Monitor blood glucose during concomitant sulfonylurea and angiotensin receptor blocker use. Concomitant use may cause an increased blood glucose-lowering effect with risk of hypoglycemia.
Olmesartan; Amlodipine; Hydrochlorothiazide, HCTZ: (Moderate) Monitor blood glucose during concomitant sulfonylurea and angiotensin receptor blocker use. Concomitant use may cause an increased blood glucose-lowering effect with risk of hypoglycemia.
Olmesartan; Hydrochlorothiazide, HCTZ: (Moderate) Monitor blood glucose during concomitant sulfonylurea and angiotensin receptor blocker use. Concomitant use may cause an increased blood glucose-lowering effect with risk of hypoglycemia.
Omadacycline: (Moderate) Additive photosensitization may be seen with concurrent administration of sulfonylureas and other photosensitizing agents including tetracyclines. Prevention of photosensitivity includes adequate protection from sources of UV radiation (e.g., avoiding sun exposure and tanning booths) and the use of protective clothing and sunscreens on exposed skin.
Ombitasvir; Paritaprevir; Ritonavir: (Moderate) New onset diabetes mellitus, exacerbation of diabetes mellitus, and hyperglycemia due to insulin resistance have been reported with use of anti-retroviral protease inhibitors. A possible mechanism is impairment of beta-cell function. Onset averaged approximately 63 days after initiating protease inhibitor therapy, but has occurred as early as 4 days after beginning therapy. Diabetic ketoacidosis has occurred in some patients including patients who were not diabetic prior to protease inhibitor treatment. Patients on antidiabetic agents should be closely monitored for changes in glycemic control, specifically hyperglycemia, if protease inhibitor therapy is initiated.
Oritavancin: (Moderate) Chlorpropamide is metabolized by CYP2C9; oritavancin is a weak CYP2C9 inhibitor. Coadministration may result in elevated chlorpropamide plasma concentrations. If these drugs are administered concurrently, blood glucose should be monitored closely.
Orlistat: (Minor) Weight-loss may affect glycemic control in patients with diabetes mellitus. In many patients, glycemic control may improve. A reduction in dose of oral hypoglycemic medications may be required in some patients taking orlistat. Monitor blood glucose and glycemic control and adjust therapy as clinically indicated.
Oxandrolone: (Moderate) Changes in insulin sensitivity or glycemic control may occur in patients treated with androgens. In diabetic patients, the metabolic effects of androgens may decrease blood glucose and, therefore, may decrease antidiabetic agent dosage requirements. Monitor blood glucose and HbA1C when these drugs are used together.
Oxymetholone: (Moderate) Changes in insulin sensitivity or glycemic control may occur in patients treated with androgens. In diabetic patients, the metabolic effects of androgens may decrease blood glucose and, therefore, may decrease antidiabetic agent dosage requirements. Monitor blood glucose and HbA1C when these drugs are used together.
Paliperidone: (Moderate) Atypical antipsychotic therapy may aggravate diabetes mellitus and cause metabolic changes such as hyperglycemia. Monitor patients on antidiabetic agents for worsening glycemic control. The atypical antipsychotics have been associated with metabolic changes, including hyperglycemia, diabetic ketoacidosis, hyperosmolar, hyperglycemic states, and diabetic coma. Aggravation of diabetes mellitus has been reported. Possible mechanisms include atypical antipsychotic-

induced insulin resistance or direct beta-cell inhibition.
Pasireotide: (Moderate) Monitor blood glucose levels regularly in patients with diabetes, especially when pasireotide treatment is initiated or when the dose is altered. Adjust treatment with antidiabetic agents as clinically indicated. Pasireotide inhibits the secretion of insulin and glucagon. Patients treated with pasireotide may experience either hypoglycemia or hyperglycemia.
Pegvisomant: (Moderate) Monitor blood glucose levels regularly in patients with diabetes, especially when pegvisomant treatment is initiated or when the dose is altered. Adjust treatment with antidiabetic agents as clinically indicated. Pegvisomant increases sensitivity to insulin by lowering the activity of growth hormone, and in some patients glucose tolerance improves with treatment. Patients with diabetes treated with pegvisomant and antidiabetic agents may be more likely to experience hypoglycemia.
Pemoline: (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.
Penbutolol: (Moderate) Increased frequency of blood glucose monitoring may be required when a beta blocker is given with antidiabetic agents. Since beta blockers inhibit the release of catecholamines, these medications may hide symptoms of hypoglycemia such as tremor, tachycardia, and blood pressure changes. Other symptoms, like headache, dizziness, nervousness, mood changes, or hunger are not blunted. Beta-blockers also exert complex actions on the body's ability to regulate blood glucose. Some beta-blockers, particularly non-selective beta-blockers such as propranolol, have been noted to potentiate insulin-induced hypoglycemia and a delay in recovery of blood glucose to normal levels. Hyperglycemia has been reported as well and is possibly due to beta-2 receptor blockade in the beta cells of the pancreas. A selective beta-blocker may be preferred in patients with diabetes mellitus, if appropriate for the patient's condition. Selective beta-blockers, such as atenolol or metoprolol, do not appear to potentiate insulin-induced hypoglycemia. While beta-blockers may have negative effects on glycemic control, they reduce the risk of cardiovascular disease and stroke in patients with diabetes and their use should not be avoided in patients with compelling indications for beta-blocker therapy when no other contraindications are present.
Pentamidine: (Moderate) Pentamidine can be harmful to pancreatic cells. This effect may lead to hypoglycemia acutely, followed by hyperglycemia with prolonged pentamidine therapy. Patients on antidiabetic agents should be monitored for the need for dosage adjustments during the use of pentamidine.
Pentoxifylline: (Moderate) Pentoxiphylline has been used concurrently with antidiabetic agents without observed problems, but it may enhance the hypoglycemic action of antidiabetic agents. Patients should be monitored for changes in glycemic control while receiving pentoxifylline in combination with antidiabetic agents.
Perindopril: (Moderate) Monitor blood glucose during concomitant sulfonylurea and angiotensin-converting enzyme (ACE) inhibitor use. Concomitant use may cause an increased blood glucose-lowering effect with risk of hypoglycemia.
Perindopril; Amlodipine: (Moderate) Monitor blood glucose during concomitant sulfonylurea and angiotensin-converting enzyme (ACE) inhibitor use. Concomitant use may cause an increased blood glucose-lowering effect with risk of hypoglycemia.
Phendimetrazine: (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.
Phenelzine: (Moderate) Monitor blood glucose during concomitant sulfonylurea and monoamine oxidase inhibitor (MAOI) use; a sulfonylurea dose adjustment may be necessary. Concomitant use may cause an increased blood glucose-lowering effect with risk of hypoglycemia.
Phenothiazines: (Moderate) Phenothiazines, especially chlorpromazine, may increase blood glucose concentrations. Hyperglycemia and glycosuria have been reported. Patients who are taking antidiabetic agents should monitor for worsening glycemic control when a phenothiazine is instituted. Also, concomitant use may increase the risk for phototoxicity. Patients should take care and use proper techniques to limit sunlight and UV exposure.
Phentermine: (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.
Phentermine; Topiramate: (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.
Phenylephrine: (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.
Phenytoin: (Minor) Phenytoin and other hydantoins have the potential to increase blood glucose and thus interact with antidiabetic agents pharmacodynamically. In addition, coadministration may result in decreased serum concentrations of chlorpropamide. Monitor blood glucose for changes in glycemic control. Dosage adjustments may be necessary in some patients.
Photosensitizing agents (topical): (Moderate) Additive photosensitization may be seen with concurrent administration of sulfonylureas and other photosensitizing agents. Prevention of photosensitivity includes adequate protection from sources of UV radiation (e.g., avoiding sun exposure and tanning booths) and the use of protective clothing and sunscreens on exposed skin
Pindolol: (Moderate) Increased frequency of blood glucose monitoring may be required when a beta blocker is given with antidiabetic agents. Since beta blockers inhibit the release of catecholamines, these medications may hide symptoms of hypoglycemia such as tremor, tachycardia, and blood pressure

changes. Other symptoms, like headache, dizziness, nervousness, mood changes, or hunger are not blunted. Beta-blockers also exert complex actions on the body's ability to regulate blood glucose. Some beta-blockers, particularly non-selective beta-blockers such as propranolol, have been noted to potentiate insulin-induced hypoglycemia and a delay in recovery of blood glucose to normal levels. Hyperglycemia has been reported as well and is possibly due to beta-2 receptor blockade in the beta cells of the pancreas. A selective beta-blocker may be preferred in patients with diabetes mellitus, if appropriate for the patient's condition. Selective beta-blockers, such as atenolol or metoprolol, do not appear to potentiate insulin-induced hypoglycemia. While beta-blockers may have negative effects on glycemic control, they reduce the risk of cardiovascular disease and stroke in patients with diabetes and their use should not be avoided in patients with compelling indications for beta-blocker therapy when no other contraindications are present.
Pioglitazone: (Moderate) If hypoglycemia occurs during concomitant use of pioglitazone and a sulfonylurea, reduce the dose of the sulfonylurea. Patients receiving pioglitazone in combination with sulfonylureas may be at risk for hypoglycemia.
Pioglitazone; Glimepiride: (Moderate) If hypoglycemia occurs during concomitant use of pioglitazone and a sulfonylurea, reduce the dose of the sulfonylurea. Patients receiving pioglitazone in combination with sulfonylureas may be at risk for hypoglycemia.
Pioglitazone; Metformin: (Moderate) If hypoglycemia occurs during concomitant use of pioglitazone and a sulfonylurea, reduce the dose of the sulfonylurea. Patients receiving pioglitazone in combination with sulfonylureas may be at risk for hypoglycemia. (Moderate) Monitor blood glucose during concomitant sulfonylurea and metformin use; a sulfonylurea dose adjustment may be necessary. Concomitant use may cause an increased blood glucose-lowering effect with risk of hypoglycemia.
Porfimer: (Major) Avoid coadministration of porfimer with sulfonylureas due to the risk of increased photosensitivity. Porfimer is a light-activated drug used in photodynamic therapy; all patients treated with porfimer will be photosensitive. Concomitant use of other photosensitizing agents like sulfonylureas may increase the risk of a photosensitivity reaction.
Potassium Bicarbonate: (Moderate) Urinary alkalinizing agents, like potassium citrate, may increase the excretion of chlorpropamide by increasing renal clearance. Monitor for decreased efficacy of chlorpropamide (i.e., increased blood glucose) during coadministration.
Potassium Chloride: (Moderate) Urinary alkalinizing agents, like potassium citrate, may increase the excretion of chlorpropamide by increasing renal clearance. Monitor for decreased efficacy of chlorpropamide (i.e., increased blood glucose) during coadministration.
Potassium Citrate: (Moderate) Urinary alkalinizing agents, like potassium citrate, may increase the excretion of chlorpropamide by increasing renal clearance. Monitor for decreased efficacy of chlorpropamide (i.e., increased blood glucose) during coadministration.
Potassium Citrate; Citric Acid: (Moderate) Urinary alkalinizing agents, like potassium citrate, may increase the excretion of chlorpropamide by increasing renal clearance. Monitor for decreased efficacy of chlorpropamide (i.e., increased blood glucose) during coadministration.
Prasterone, Dehydroepiandrosterone, DHEA (Dietary Supplements): (Moderate) Changes in insulin sensitivity or glycemic control may occur in patients treated with androgens. In diabetic patients, the metabolic effects of androgens may decrease blood glucose and, therefore, may decrease antidiabetic agent dosage requirements. Monitor blood glucose and HbA1C when these drugs are used together.
Prasterone, Dehydroepiandrosterone, DHEA (FDA-approved): (Moderate) Changes in insulin sensitivity or glycemic control may occur in patients treated with androgens. In diabetic patients, the metabolic effects of androgens may decrease blood glucose and, therefore, may decrease antidiabetic agent dosage requirements. Monitor blood glucose and HbA1C when these drugs are used together.
Prilocaine; Epinephrine: (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.
Probenecid: (Moderate) Probenecid is highly protein bound, and the hypoglycemic effect of sulfonylureas made be potentiated if these drugs are coadministered.
Probenecid; Colchicine: (Moderate) Probenecid is highly protein bound, and the hypoglycemic effect of sulfonylureas made be potentiated if these drugs are coadministered.
Progestins: (Minor) Progestins can impair glucose tolerance. Patients receiving antidiabetic agents should be closely monitored for signs indicating changes in diabetic control when therapy with progestins is instituted or discontinued.
Promethazine; Phenylephrine: (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.
Propranolol: (Moderate) Increased frequency of blood glucose monitoring may be required when a beta blocker is given with antidiabetic agents. Since beta blockers inhibit the release of catecholamines, these medications may hide symptoms of hypoglycemia such as tremor, tachycardia, and blood pressure changes. Other symptoms, like headache, dizziness, nervousness, mood changes, or hunger are not blunted. Beta-blockers also exert complex actions on the body's ability to regulate blood glucose. Some beta-blockers, particularly non-selective beta-blockers such as propranolol, have been noted to potentiate insulin-induced hypoglycemia and a delay in recovery of blood glucose to normal levels. Hyperglycemia has been reported as well and is possibly due to beta-2 receptor blockade in the beta cells of the pancreas. A selective beta-blocker may be preferred in patients with diabetes mellitus, if appropriate for the patient's condition. Selective beta-blockers, such as atenolol or metoprolol, do not appear to potentiate insulin-induced hypoglycemia. While beta-blockers may have negative effects on glycemic control, they reduce the risk of cardiovascular disease and stroke in patients with diabetes and their use should not be avoided in patients with compelling indications for beta-blocker therapy when no other contraindications are present.
Propranolol; Hydrochlorothiazide, HCTZ: (Moderate) Increased frequency of blood glucose monitoring may be required when a beta blocker is given with antidiabetic agents. Since beta blockers inhibit the release of catecholamines, these medications may hide symptoms of hypoglycemia such as tremor, tachycardia, and blood pressure changes. Other symptoms, like headache, dizziness, nervousness, mood changes, or hunger are not blunted. Beta-blockers also exert complex actions on the body's ability to regulate blood glucose. Some beta-blockers, particularly non-selective beta-blockers such as propranolol, have been noted to potentiate insulin-induced hypoglycemia and a delay in recovery of blood glucose to normal levels. Hyperglycemia has been reported as well and is possibly due to beta-2 receptor blockade in the beta cells of the pancreas. A selective beta-blocker may be preferred in patients with diabetes mellitus, if appropriate for the patient's condition. Selective beta-blockers, such as atenolol or metoprolol, do not appear to potentiate insulin-induced hypoglycemia. While beta-blockers may have negative effects on glycemic control, they reduce the risk of cardiovascular disease and stroke in patients with diabetes and their use should not be avoided in patients with compelling indications for beta-blocker therapy when no

other contraindications are present.
Protease inhibitors: (Moderate) New onset diabetes mellitus, exacerbation of diabetes mellitus, and hyperglycemia due to insulin resistance have been reported with use of anti-retroviral protease inhibitors. A possible mechanism is impairment of beta-cell function. Onset averaged approximately 63 days after initiating protease inhibitor therapy, but has occurred as early as 4 days after beginning therapy. Diabetic ketoacidosis has occurred in some patients including patients who were not diabetic prior to protease inhibitor treatment. Patients on antidiabetic agents should be closely monitored for changes in glycemic control, specifically hyperglycemia, if protease inhibitor therapy is initiated.
Pseudoephedrine: (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.
Pseudoephedrine; Triprolidine: (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.
Quetiapine: (Moderate) Atypical antipsychotic therapy may aggravate diabetes mellitus and cause metabolic changes such as hyperglycemia. Monitor patients on antidiabetic agents for worsening glycemic control. The atypical antipsychotics have been associated with metabolic changes, including hyperglycemia, diabetic ketoacidosis, hyperosmolar, hyperglycemic states, and diabetic coma. Aggravation of diabetes mellitus has been reported. Possible mechanisms include atypical antipsychotic-induced insulin resistance or direct beta-cell inhibition.
Quinapril: (Moderate) Monitor blood glucose during concomitant sulfonylurea and angiotensin-converting enzyme (ACE) inhibitor use. Concomitant use may cause an increased blood glucose-lowering effect with risk of hypoglycemia.
Quinapril; Hydrochlorothiazide, HCTZ: (Moderate) Monitor blood glucose during concomitant sulfonylurea and angiotensin-converting enzyme (ACE) inhibitor use. Concomitant use may cause an increased blood glucose-lowering effect with risk of hypoglycemia.
Quinolones: (Moderate) Monitor blood glucose during concomitant sulfonylurea and quinolone use. Concomitant use may cause an increased blood glucose-lowering effect with risk of hypoglycemia.
Racepinephrine: (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.
Ramipril: (Moderate) Monitor blood glucose during concomitant sulfonylurea and angiotensin-converting enzyme (ACE) inhibitor use. Concomitant use may cause an increased blood glucose-lowering effect with

risk of hypoglycemia.
Ranitidine: (Moderate) Ranitidine has been shown to affect the pharmacokinetics of some oral sulfonylureas. Patients receiving sulfonylureas should be observed for evidence of altered glycemic response when ranitidine is instituted or discontinued. The mechanism of this interaction may involve either increasing the absorption or decreasing the clearance of the sulfonylurea. Asymptomatic hypoglycemia has been observed as a result of this interaction. It is unclear at this time if famotidine or nizatidine interact with oral sulfonylureas.
Relugolix; Estradiol; Norethindrone acetate: (Minor) Patients receiving antidiabetic agents should be periodically monitored for changes in glycemic control when hormone therapy is instituted or discontinued. Estrogens can decrease the hypoglycemic effects of antidiabetic agents by impairing glucose tolerance. Changes in glucose tolerance occur more commonly in patients receiving 50 mcg or more of ethinyl estradiol (or equivalent) per day in combined oral contraceptives (COCs), which are not commonly used in practice since the marketing of lower dose COCs, patches, injections and rings. The presence or absence of a concomitant progestin may influence the significance of any hormonal effect on glucose homeostasis.
Reserpine: (Moderate) Reserpine may mask the signs and symptoms of hypoglycemia. Patients receiving reserpine concomitantly with antidiabetic agents should be monitored for changes in glycemic control.
Rifamycins: (Moderate) Monitor for decreased efficacy of sulfonylureas during coadministration of rifamycins as plasma concentrations of sulfonylureas may be decreased; dosage adjustments made be necessary. Sulfonylureas are CYP2C9 substrates and rifamycins are CYP2C9 inducers.
Risperidone: (Moderate) Atypical antipsychotic therapy may aggravate diabetes mellitus and cause metabolic changes such as hyperglycemia. Monitor patients on antidiabetic agents for worsening glycemic control. The atypical antipsychotics have been associated with metabolic changes, including hyperglycemia, diabetic ketoacidosis, hyperosmolar, hyperglycemic states, and diabetic coma. Aggravation of diabetes mellitus has been reported. Possible mechanisms include atypical antipsychotic-induced insulin resistance or direct beta-cell inhibition.
Ritodrine: (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.
Ritonavir: (Moderate) New onset diabetes mellitus, exacerbation of diabetes mellitus, and hyperglycemia due to insulin resistance have been reported with use of anti-retroviral protease inhibitors. A possible mechanism is impairment of beta-cell function. Onset averaged approximately 63 days after initiating protease inhibitor therapy, but has occurred as early as 4 days after beginning therapy. Diabetic ketoacidosis has occurred in some patients including patients who were not diabetic prior to protease inhibitor treatment. Patients on antidiabetic agents should be closely monitored for changes in glycemic control, specifically hyperglycemia, if protease inhibitor therapy is initiated.
Rosiglitazone: (Major) A maximum dose of 8 mg/day of rosiglitazone is recommended when used in combination with sulfonylureas; the incidence of adverse effects including hypoglycemia is increased with larger doses. In one clinical study, rosiglitazone 4 or 8 mg/day was added to failed glimepiride plus metformin therapy. The incidence of hypoglycemia (blood glucose concentrations <= 50 mg/dl) was 18.6% in the 4 mg/day group compared with 28% in the 8 mg/day group. In addition, 4 or 8 mg/day of rosiglitazone has been added to failed glyburide plus metformin therapy. The incidence of hypoglycemia was higher in the rosiglitazone (average dose 7.4 mg/day)+glyburide+metformin group (22%) when

compared to the glyburide+metformin group (3%). Patients should be instructed to monitor blood glucose concentrations more frequently. Dosage adjustments may be indicated.
Sacubitril; Valsartan: (Moderate) Monitor blood glucose during concomitant sulfonylurea and angiotensin receptor blocker use. Concomitant use may cause an increased blood glucose-lowering effect with risk of hypoglycemia.
Salsalate: (Moderate) If salicylates and sulfonylureas are to be administered together, patients should be monitored for changes in glycemic control. Salicylates, by inhibiting prostaglandin E2 synthesis, can indirectly increase insulin secretion. Thus, salicylates can decrease blood sugar and may potentiate the effects of other antidiabetic agents. This mechanism may explain how salicylates can potentiate the clinical effects of sulfonylureas; however, displacement of sulfonylureas from protein binding sites has also been reported. In large doses, salicylates uncouple oxidative phosphorylation, deplete hepatic and muscle glycogen, and cause hyperglycemia and glycosuria.
Saquinavir: (Moderate) New onset diabetes mellitus, exacerbation of diabetes mellitus, and hyperglycemia due to insulin resistance have been reported with use of anti-retroviral protease inhibitors. A possible mechanism is impairment of beta-cell function. Onset averaged approximately 63 days after initiating protease inhibitor therapy, but has occurred as early as 4 days after beginning therapy. Diabetic ketoacidosis has occurred in some patients including patients who were not diabetic prior to protease inhibitor treatment. Patients on antidiabetic agents should be closely monitored for changes in glycemic control, specifically hyperglycemia, if protease inhibitor therapy is initiated.
Sarecycline: (Moderate) Additive photosensitization may be seen with concurrent administration of sulfonylureas and other photosensitizing agents including tetracyclines. Prevention of photosensitivity includes adequate protection from sources of UV radiation (e.g., avoiding sun exposure and tanning booths) and the use of protective clothing and sunscreens on exposed skin.
Saxagliptin: (Moderate) A lower sulfonylurea dose may be required when used in combination with saxagliptin to minimize the risk of hypoglycemia. When saxagliptin was used in combination with a sulfonylurea, the incidence of hypoglycemia was increased compared to a placebo used in combination with a sulfonylurea.
Segesterone Acetate; Ethinyl Estradiol: (Minor) Patients receiving antidiabetic agents should be periodically monitored for changes in glycemic control when hormone therapy is instituted or discontinued. Estrogens can decrease the hypoglycemic effects of antidiabetic agents by impairing glucose tolerance. Changes in glucose tolerance occur more commonly in patients receiving 50 mcg or more of ethinyl estradiol (or equivalent) per day in combined oral contraceptives (COCs), which are not commonly used in practice since the marketing of lower dose COCs, patches, injections and rings. The presence or absence of a concomitant progestin may influence the significance of any hormonal effect on glucose homeostasis.
Semaglutide: (Moderate) Monitor blood glucose during concomitant sulfonylurea and semaglutide use; consider decreasing the sulfonylurea dose when starting semaglutide. Concomitant use may cause an increased blood glucose-lowering effect with risk of hypoglycemia.
Serdexmethylphenidate; Dexmethylphenidate: (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.
Sofosbuvir: (Moderate) Closely monitor blood glucose levels if sofosbuvir is administered with antidiabetic agents. Dose adjustments of the antidiabetic agents may be needed. Altered blood glucose

control, resulting in serious symptomatic hypoglycemia, has been reported in diabetic patients receiving antidiabetic agents in combination with direct acting antivirals, such as sofosbuvir.
Sofosbuvir; Velpatasvir: (Moderate) Closely monitor blood glucose levels if sofosbuvir is administered with antidiabetic agents. Dose adjustments of the antidiabetic agents may be needed. Altered blood glucose control, resulting in serious symptomatic hypoglycemia, has been reported in diabetic patients receiving antidiabetic agents in combination with direct acting antivirals, such as sofosbuvir. (Moderate) Closely monitor blood glucose levels if velpatasvir is administered with antidiabetic agents. Dose adjustments of the antidiabetic agents may be needed. Altered blood glucose control, resulting in serious symptomatic hypoglycemia, has been reported in diabetic patients receiving antidiabetic agents in combination with direct acting antivirals, such as velpatasvir.
Sofosbuvir; Velpatasvir; Voxilaprevir: (Moderate) Closely monitor blood glucose levels if sofosbuvir is administered with antidiabetic agents. Dose adjustments of the antidiabetic agents may be needed. Altered blood glucose control, resulting in serious symptomatic hypoglycemia, has been reported in diabetic patients receiving antidiabetic agents in combination with direct acting antivirals, such as sofosbuvir. (Moderate) Closely monitor blood glucose levels if velpatasvir is administered with antidiabetic agents. Dose adjustments of the antidiabetic agents may be needed. Altered blood glucose control, resulting in serious symptomatic hypoglycemia, has been reported in diabetic patients receiving antidiabetic agents in combination with direct acting antivirals, such as velpatasvir. (Moderate) Closely monitor blood glucose levels if voxilaprevir is administered with antidiabetic agents. Dose adjustments of the antidiabetic agents may be needed. Altered blood glucose control, resulting in serious symptomatic hypoglycemia, has been reported in diabetic patients receiving antidiabetic agents in combination with direct acting antivirals, such as voxilaprevir.
Somatropin, rh-GH: (Moderate) Patients with diabetes mellitus should be monitored closely during somatropin (recombinant rhGH) therapy. Antidiabetic drugs (e.g., insulin or oral agents) may require adjustment when somatropin therapy is instituted in these patients. Growth hormones, such as somatropin, may decrease insulin sensitivity, leading to glucose intolerance and loss of blood glucose control. Therefore, glucose levels should be monitored periodically in all patients treated with somatropin, especially in those with risk factors for diabetes mellitus.
Sotalol: (Moderate) Increased frequency of blood glucose monitoring may be required when a beta blocker is given with antidiabetic agents. Since beta blockers inhibit the release of catecholamines, these medications may hide symptoms of hypoglycemia such as tremor, tachycardia, and blood pressure changes. Other symptoms, like headache, dizziness, nervousness, mood changes, or hunger are not blunted. Beta-blockers also exert complex actions on the body's ability to regulate blood glucose. Some beta-blockers, particularly non-selective beta-blockers such as propranolol, have been noted to potentiate insulin-induced hypoglycemia and a delay in recovery of blood glucose to normal levels. Hyperglycemia has been reported as well and is possibly due to beta-2 receptor blockade in the beta cells of the pancreas. A selective beta-blocker may be preferred in patients with diabetes mellitus, if appropriate for the patient's condition. Selective beta-blockers, such as atenolol or metoprolol, do not appear to potentiate insulin-induced hypoglycemia. While beta-blockers may have negative effects on glycemic control, they reduce the risk of cardiovascular disease and stroke in patients with diabetes and their use should not be avoided in patients with compelling indications for beta-blocker therapy when no other contraindications are present.
Sulfacetamide: (Moderate) Sulfonamides may cause photosensitization and may increase the photosensitizing effects of sulfonylureas. Patients should take care and use proper techniques to limit sunlight and UV exposure of treated areas.
Sulfacetamide; Sulfur: (Moderate) Sulfonamides may cause photosensitization and may increase the photosensitizing effects of sulfonylureas. Patients should take care and use proper techniques to limit sunlight and UV exposure of treated areas.

Sulfinpyrazone: (Moderate) Sulfinpyrazone is an inhibitor of CYP2C9. Sulfinpyrazone may inhibit the hepatic metabolism of sulfonylureas, CYP2C9 substrates. Patients should be monitored for an increased hypoglycemic effect.
Sulfonamides: (Moderate) Sulfonamides may enhance the hypoglycemic action of antidiabetic agents; patients with diabetes mellitus should be closely monitored during sulfonamide treatment. Taking these drugs together may also increase risk for phototoxicity. Patients should limit sunlight and UV exposure, and follow proper precautions for sunscreens and protective clothing. Sulfonamides may induce hypoglycemia in some patients by increasing the secretion of insulin from the pancreas. Patients at risk for hypoglycemia due to sulfonamides include those with compromised renal function, those fasting for prolonged periods, those that are malnourished, and those receiving high or excessive doses of sulfonamides.
Sympathomimetics: (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.
Tacrolimus: (Moderate) Tacrolimus has been reported to cause hyperglycemia and has been implicated in causing insulin-dependent diabetes mellitus in patients after renal transplantation. Tacrolimus may have direct beta-cell toxicity. Patients should be monitored for worsening of glycemic control if therapy with tacrolimus is initiated in patients receiving antidiabetic agents.
Tazarotene: (Moderate) The manufacturer states that tazarotene should be administered with caution in patients who are also taking drugs known to be photosensitizers, such as sulfonylureas, as concomitant use may augment phototoxicity. Patients should take care and use proper techniques to limit sunlight and UV exposure of treated areas.
Tegaserod: (Moderate) Tegaserod can enhance gastric emptying in diabetic patients, blood glucose can be affected, which, in turn, may affect the clinical response to antidiabetic agents. The dosing of antidiabetic agents may require adjustment in patients who receive GI prokinetic agents concomitantly.
Telmisartan: (Moderate) Monitor blood glucose during concomitant sulfonylurea and angiotensin receptor blocker use. Concomitant use may cause an increased blood glucose-lowering effect with risk of hypoglycemia.
Telmisartan; Amlodipine: (Moderate) Monitor blood glucose during concomitant sulfonylurea and angiotensin receptor blocker use. Concomitant use may cause an increased blood glucose-lowering effect with risk of hypoglycemia.
Telmisartan; Hydrochlorothiazide, HCTZ: (Moderate) Monitor blood glucose during concomitant sulfonylurea and angiotensin receptor blocker use. Concomitant use may cause an increased blood glucose-lowering effect with risk of hypoglycemia.
Testosterone: (Moderate) Changes in insulin sensitivity or glycemic control may occur in patients treated with androgens. In diabetic patients, the metabolic effects of androgens may decrease blood glucose and, therefore, may decrease antidiabetic agent dosage requirements. Monitor blood glucose and HbA1C when these drugs are used together.
Tetracycline: (Moderate) Additive photosensitization may be seen with concurrent administration of sulfonylureas and other photosensitizing agents including tetracyclines. Prevention of photosensitivity includes adequate protection from sources of UV radiation (e.g., avoiding sun exposure and tanning booths) and the use of protective clothing and sunscreens on exposed skin.
Tetracyclines: (Moderate) Additive photosensitization may be seen with concurrent administration of

sulfonylureas and other photosensitizing agents including tetracyclines. Prevention of photosensitivity includes adequate protection from sources of UV radiation (e.g., avoiding sun exposure and tanning booths) and the use of protective clothing and sunscreens on exposed skin.
Thiazide diuretics: (Moderate) Thiazide diuretics can decrease insulin sensitivity thereby leading to glucose intolerance and hyperglycemia. Diuretic-induced hypokalemia may also lead to hyperglycemia. Because of this, a potential pharmacodynamic interaction exists between thiazide diuretics and antidiabetic agents. It appears that the effects of thiazide diuretics on glycemic control are dose-related and low doses can be instituted without deleterious effects on glycemic control. In addition, diuretics reduce the risk of stroke and cardiovascular disease in patients with diabetes. However, patients taking antidiabetic agents should be monitored for changes in blood glucose control if such diuretics are added or deleted. Dosage adjustments may be necessary.
Thyroid hormones: (Minor) Addition of thyroid hormones to antidiabetic or insulin therapy may result in increased dosage requirements of the antidiabetic agents. Blood sugars should be carefully monitored when thyroid therapy is added, discontinued or doses changed.
Timolol: (Moderate) Increased frequency of blood glucose monitoring may be required when a beta blocker is given with antidiabetic agents. Since beta blockers inhibit the release of catecholamines, these medications may hide symptoms of hypoglycemia such as tremor, tachycardia, and blood pressure changes. Other symptoms, like headache, dizziness, nervousness, mood changes, or hunger are not blunted. Beta-blockers also exert complex actions on the body's ability to regulate blood glucose. Some beta-blockers, particularly non-selective beta-blockers such as propranolol, have been noted to potentiate insulin-induced hypoglycemia and a delay in recovery of blood glucose to normal levels. Hyperglycemia has been reported as well and is possibly due to beta-2 receptor blockade in the beta cells of the pancreas. A selective beta-blocker may be preferred in patients with diabetes mellitus, if appropriate for the patient's condition. Selective beta-blockers, such as atenolol or metoprolol, do not appear to potentiate insulin-induced hypoglycemia. While beta-blockers may have negative effects on glycemic control, they reduce the risk of cardiovascular disease and stroke in patients with diabetes and their use should not be avoided in patients with compelling indications for beta-blocker therapy when no other contraindications are present.
Tipranavir: (Moderate) New onset diabetes mellitus, exacerbation of diabetes mellitus, and hyperglycemia due to insulin resistance have been reported with use of anti-retroviral protease inhibitors. A possible mechanism is impairment of beta-cell function. Onset averaged approximately 63 days after initiating protease inhibitor therapy, but has occurred as early as 4 days after beginning therapy. Diabetic ketoacidosis has occurred in some patients including patients who were not diabetic prior to protease inhibitor treatment. Patients on antidiabetic agents should be closely monitored for changes in glycemic control, specifically hyperglycemia, if protease inhibitor therapy is initiated.
Tirzepatide: (Moderate) When tirzepatide is used with insulin secretagogues such as the sulfonylureas, consider lowering the dose of the sulfonylureas to reduce the risk of hypoglycemia and monitor the blood glucose concentration more frequently. Patients receiving tirzepatide in combination with sulfonylureas may have an increased risk of hypoglycemia, including severe hypoglycemia.
Torsemide: (Minor) Hyperglycemia has been detected during torsemide therapy, but the incidence is low. Because of this, a potential pharmacodynamic interaction exists between torsemide and all antidiabetic agents. Monitor blood glucose.
Trandolapril: (Moderate) Monitor blood glucose during concomitant sulfonylurea and angiotensin-converting enzyme (ACE) inhibitor use. Concomitant use may cause an increased blood glucose-lowering effect with risk of hypoglycemia.
Trandolapril; Verapamil: (Moderate) Monitor blood glucose during concomitant sulfonylurea and angiotensin-converting enzyme (ACE) inhibitor use. Concomitant use may cause an increased blood glucose-lowering effect with risk of hypoglycemia.

Tranylcypromine: (Moderate) Monitor blood glucose during concomitant sulfonylurea and monoamine oxidase inhibitor (MAOI) use; a sulfonylurea dose adjustment may be necessary. Concomitant use may cause an increased blood glucose-lowering effect with risk of hypoglycemia.
Tretinoin, ATRA: (Moderate) A manufacturer of topical tretinoin states that tretinoin, ATRA should be administered with caution in patients who are also taking drugs known to be photosensitizers, such as sulfonylureas, as concomitant use may augment phototoxicity. Patients should take care and use proper techniques to limit sunlight and UV exposure of treated areas.
Tretinoin; Benzoyl Peroxide: (Moderate) A manufacturer of topical tretinoin states that tretinoin, ATRA should be administered with caution in patients who are also taking drugs known to be photosensitizers, such as sulfonylureas, as concomitant use may augment phototoxicity. Patients should take care and use proper techniques to limit sunlight and UV exposure of treated areas.
Triamterene: (Minor) Triamterene can interfere with the hypoglycemic effects of antidiabetic agents. This can lead to a loss of diabetic control, so diabetic patients should be monitored closely.
Triamterene; Hydrochlorothiazide, HCTZ: (Minor) Triamterene can interfere with the hypoglycemic effects of antidiabetic agents. This can lead to a loss of diabetic control, so diabetic patients should be monitored closely.
Valsartan: (Moderate) Monitor blood glucose during concomitant sulfonylurea and angiotensin receptor blocker use. Concomitant use may cause an increased blood glucose-lowering effect with risk of hypoglycemia.
Valsartan; Hydrochlorothiazide, HCTZ: (Moderate) Monitor blood glucose during concomitant sulfonylurea and angiotensin receptor blocker use. Concomitant use may cause an increased blood glucose-lowering effect with risk of hypoglycemia.
Vasopressin, ADH: (Moderate) Monitor hemodynamics and adjust the dose of vasopressin as needed when used concomitantly with drugs suspected of causing syndrome of inappropriate antidiuretic hormone (SIADH), such as chlorpropamide. Use together may increase the pressor and antidiuretic effects of vasopressin.
Verteporfin: (Moderate) Use caution if coadministration of verteporfin with sulfonylureas is necessary due to the risk of increased photosensitivity. Verteporfin is a light-activated drug used in photodynamic therapy; all patients treated with verteporfin will be photosensitive. Concomitant use of other photosensitizing agents like sulfonylureas may increase the risk of a photosensitivity reaction.
Vonoprazan; Amoxicillin; Clarithromycin: (Moderate) The concomitant use of clarithromycin and antidiabetic agents can result in significant hypoglycemia. Careful monitoring of blood glucose is recommended.
Voriconazole: (Moderate) Voriconazole should be used cautiously with sulfonylureas. The combination of voriconazole and oral antidiabetic agents may result in severe hypoglycemia. Voriconazole may inhibit the metabolism of sulfonylureas. Blood glucose concentrations should be monitored and possible dose adjustments of hypoglycemics may need to be made.
Warfarin: (Moderate) The interaction between oral anticoagulants and oral sulfonylureas is complex; both enhancement or reduction of hypoprothrombinemic response to oral anticoagulants has been reported in various literature accounts along with a potential for altered hypoglycemic response to the sulfonylurea. One proposed mechanism may be related to displacement of the drugs from plasma protein binding sites. Dicumarol has been reported to inhibit the metabolism of chlorpropamide and tolbutamide, however, warfarin did not exhibit a similar effect on tolbutamide kinetics. Glyburide has been reported to augment the hypoprothrombinemic response to warfarin, although other reports have showed no interaction. Warfarin appears less likely to interact with sulfonylureas than dicumarol. In clinical trials, glimepiride therapy resulted in a slight, but statistically significant decrease in pharmacodynamic response to warfarin. The reductions in effect are unlikely to be clinically important in most cases. Nevertheless, it would be wise for clinicians to use warfarin and sulfonylureas together cautiously until the combined effects of the

drugs are known. Monitor the INR as indicated and be alert for altered blood sugar control when either of these drugs is added or discontinued.
Ziprasidone: (Moderate) Atypical antipsychotic therapy may aggravate diabetes mellitus and cause metabolic changes such as hyperglycemia. Monitor patients on antidiabetic agents for worsening glycemic control. The atypical antipsychotics have been associated with metabolic changes, including hyperglycemia, diabetic ketoacidosis, hyperosmolar, hyperglycemic states, and diabetic coma. Aggravation of diabetes mellitus has been reported. Possible mechanisms include atypical antipsychotic-induced insulin resistance or direct beta-cell inhibition.

PREGNANCY AND LACTATION

Pregnancy

Chlorpropamide should be given during pregnancy only if the potential benefits justify the potential risk to the patient and fetus. Animal reproduction studies have not been conducted with chlorpropamide. One surveillance study of 18 newborns who were exposed to chlorpropamide during the 1st trimester revealed no major defects, and another study found that 6 infants who were exposed in utero to chlorpropamide during the first trimester experienced congenital defects. Sulfonylureas are not likely to provide good glucose control in pregnant women who cannot be controlled on diet alone. Prolonged severe hypoglycemia (4 to 10 days) has been reported in neonates born to mothers who were receiving a sulfonylurea drug at the time of obstetric delivery. This has been reported more frequently with the use of agents with prolonged half-lives. If chlorpropamide is used during pregnancy, it should be discontinued at least 1 month before the expected delivery date and other therapies instituted to maintain blood glucose levels as close to normal as possible. Chlorpropamide, when administered near term, crosses the placenta and may persist in the neonatal serum for 4 to 6 days, due to the long half-life. Several case reports or neonatal hypoglycemia are described in the literature, while one study showed no evidence for neonatal hypoglycemia at maternal doses of 100 to 200 mg/day or more. The American College of Obstetricians and Gynecologists (ACOG) and the American Diabetes Association (ADA) continue to recommend human insulin as the standard of care in women with diabetes mellitus and gestational diabetes mellitus (GDM) requiring medical therapy; insulin does not cross the placenta.

MECHANISM OF ACTION

The hypoglycemic action of chlorpropamide is due primarily to stimulation of pancreatic islet beta-cells, which produces an increase in insulin secretion. Sulfonylureas are believed to bind to ATP-sensitive potassium-channel receptors on the pancreatic cell surface, thereby reducing potassium conductance and causing depolarization of the membrane. Depolarization stimulates calcium ion influx through voltage-sensitive calcium channels, raising intracellular concentrations of calcium ions, which induces the secretion, or exocytosis, of insulin. The drug is not effective in the absence of functioning beta-cells, as occurs in diabetes mellitus type 1, or in severe cases of diabetes mellitus type 2, but it may be effective in patients who have not responded to other agents.

Chlorpropamide also produces extrapancreatic effects that contribute to its hypoglycemic activity. These effects include reduction of basal hepatic glucose production and an enhanced peripheral sensitivity to insulin secondary to an increase in insulin receptors or changes in the events that follow insulin-receptor binding. The relative importance of each of these actions to the overall therapeutic effect of the drug will vary among oral antidiabetic agents and from patient to patient, which may account for the variability in potency that occurs in this group of drugs. Although the main effect of these antidiabetic agents appears to

be stimulation of the first phase of insulin secretion, the sulfonylureas will also stimulate the secretion of insulin throughout the duration of a meal.

PHARMACOKINETICS

Chlorpropamide is administered orally. It is 60% to 90% protein-bound. Up to 80% of an orally administered dose is metabolized in the liver. It undergoes metabolism in humans and it is excreted in the urine as unchanged drug and as hydroxylated or hydrolyzed metabolites. Within 96 hours, 80% to 90% of a single oral dose is excreted in the urine. The urinary excretion rate is increased when the urine is alkaline and decreased when it is acidic. The mean half-life of chlorpropamide is approximately 36 hours. The onset of action occurs within 1 hour, with a maximal decrease in serum glucose levels occurring within 3 to 6 hours, and the biologic duration of action is 24 to 72 hours.

Affected cytochrome P450 (CYP450) isoenzymes and drug transporters: CYP2C9
Sulfonylureas are substrates of the CYP2C9 isoenzyme; thus, coadministration with CYP2C9 inhibitors or inducers will increase or decrease, respectively, sulfonylurea concentrations.

Oral Route

Chlorpropamide is rapidly absorbed from the GI tract. Within 1 hour after a single oral dose, it is readily detectable in the blood, and maximum concentrations are attained within 2 to 4 hours.

Shelf life

3 Years from the date of manufacturing

Special precaution for storage

Store in the original package and protect from moisture

Nature and contents of container and special and special equipment for use

administration or implantation

Tablets are packaged in printed aluminium foil

Pack sizes:

Blisters pack of 10 tablets in a carton.

Special precaution for disposal and other handling

No special requirements

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