



CLASSES

Prostacyclin Analogs/Receptor Agonists for PAH

DEA CLASS

Rx

DESCRIPTION

Pharmaceutical form of prostacyclin; vasodilator and an inhibitor of platelet aggregation; improves symptoms and prolongs survival in pulmonary hypertension.

COMMON BRAND NAMES

Flolan, Veletri

HOW SUPPLIED

Epoprostenol/Epoprostenol Sodium/Flolan/Veletri Intravenous Inj Pwd F/Sol: 0.5mg, 1.5mg

DOSAGE & INDICATIONS

For the treatment of pulmonary hypertension.

For long-term intravenous treatment of adult patients with NYHA Class III or IV primary pulmonary hypertension or adults with pulmonary hypertension due to scleroderma (systemic sclerosis).

Intravenous dosage

Adults

The infusion rate is determined via a dose-ranging procedure. The infusion rate is initiated at 2 ng/kg/minute, then increased by 2 ng/kg/minute at intervals of ≥ 15 minutes until dose-limiting pharmacological effects are observed. The most common of these effects, are nausea/vomiting, headache, hypotension, and flushing. Less common adverse effects might include chest pain, anxiety, dizziness, bradycardia, dyspnea, abdominal pain, musculoskeletal pain and tachycardia. During clinical trials, the mean maximum dose before the onset of adverse effects was 8.6 \pm 0.3 ng/kg/minute. Chronic continuous infusion should be administered via a central line only, although peripheral infusions can be used until central venous access is established. The chronic infusion should be started at 4 ng/kg/minute less than the maximum tolerated infusion rate established during acute dose-ranging. If the maximum tolerated dose during acute dose-ranging was less than 5 ng/kg/minute, then one half the maximum tolerated dose during dose-ranging should be used. During clinical trials, the mean initial chronic infusion rate was 5 ng/kg/minute. Changes in the chronic infusion rate can be made based on patient response and adverse effects. In general, increases in dose should be expected. Incremental adjustments in dose should be considered if symptoms persist or recur after improving. The infusion should be increased by 1 to 2 ng/kg/minute at intervals of at least 15 minutes, in order to allow for the assessment of clinical response. After establishing the new dose, patients should be observed for several hours and their standing and supine blood pressure and heart rate should be monitored to ensure the new dose will be tolerated.

For treatment of pulmonary arterial hypertension in pediatric patients†.

Intravenous dosage

Children† and Adolescents†

Limited data are available describing the use of IV epoprostenol in pediatric patients. The most common initial dose is 1—2 ng/kg/minute IV by continuous infusion followed by dosage titration in 1—2 ng/kg/minute increments based on clinical response. Final doses are frequently higher than those used in adult patients, especially in very young children (e.g. final infusion rates of 50—80 ng/kg/minute or higher). One retrospective report describes the use of calcium channel blockers and/or IV epoprostenol in 77 patients ages 7 months—13 years with primary pulmonary hypertension. Long-term epoprostenol infusions were initiated in 31 of those patients (mean age 8 \pm 4 years) after failing to improve on conventional therapy, including digitalis, diuretics, and supplemental oxygen as needed. Following initiation and titration of epoprostenol, mean infusion rates were 78 \pm 38 ng/kg/minute at 1 year, 116 \pm 48 ng/kg/minute at 2 years, and 122 \pm 36 ng/kg/minute at 3 years. Conventional therapy was continued in all patients, and calcium channel blockers were used inconsistently. Of the 31 patients, 24 were non-responders to acute vasodilator testing, 6 were acute responders, and 1 was too unstable to test prior to therapy initiation. The authors reported clinical improvement in all 31 patients and an improvement in pulmonary artery pressure, cardiac index, and pulmonary vascular resistance compared to baseline values. An improvement in survival compared to the conventional therapy alone group was also reported.

For short-term treatment of pulmonary hypertension using inhaled (nebulized)† therapy.

Aerosolized dosage (investigational)

Adults

NOTE: Investigational use only. A small study from Germany revealed that short-term (e.g., 15 minutes) aerosolized prostacyclin (i.e., epoprostenol) effectively lowered pulmonary artery pressure and pulmonary vascular resistance compared to baseline but had less of

an impact on systemic vascular resistance than IV prostacyclin. Prostacyclin was aerosolized with room air at a pressure of 153 kPa and was delivered to a spacer connected to the afferent limb of a Y-valve mouthpiece for 15 minutes (total dose: 52—112 mcg).

For acute vasodilator testing in pulmonary hypertension diagnosis†.

Intravenous dosage

Adults

2 ng/kg/minute IV titrated by 2 ng/kg/minute every 10 to 15 minutes up to a maximum of 10 ng/kg/minute. Guidelines suggest that patients with pulmonary arterial hypertension undergo acute vasoreactivity testing with a short-acting agent in the absence of contraindications, including low systemic blood pressure, low systemic cardiac output, or the presence of functional class (FC) IV symptoms. Acute vasoreactivity is defined as a fall in mean pulmonary artery pressure (mPAP) more than 10 mmHg, to an mPAP less than 40 mmHg, with an unchanged or increased cardiac output.

†Indicates off-label use

MAXIMUM DOSAGE

Adults

Absolute maximum dosage limits have not been established; maximum doses should be based on individual clinical response.

Elderly

Absolute maximum dosage limits have not been established; maximum doses should be based on individual clinical response.

Adolescents

Safety and efficacy have not been established; maximum doses should be based on individual clinical response.

Children

Safety and efficacy have not been established; maximum doses should be based on individual clinical response.

DOSING CONSIDERATIONS

Hepatic Impairment

Specific guidelines for dosage adjustments in hepatic impairment are not available; it appears that no dosage adjustments are needed.

Renal Impairment

No dosage adjustment needed.

ADMINISTRATION

NOTE: Epoprostenol should be used by clinicians experienced in the diagnosis and treatment of primary pulmonary hypertension. Secondary causes of pulmonary hypertension should be excluded before treatment with epoprostenol.

Injectable Administration

Visually inspect parenteral products for particulate matter and discoloration prior to administration whenever solution and container permit.

Intravenous Administration

Reconstitution

Reconstitute epoprostenol according to the FDA-approved product labeling. Only prepare Flolan with the Sterile Diluent or pH 12 Sterile Diluent provided. Prepare Veletri with Sterile Water for Injection or 0.9% Sodium Chloride Injection.

Select a concentration for the epoprostenol solution that is compatible with the infusion pump being used in respect to flow rates and reservoir capacity. Solutions for chronic therapy should be prepared with a total reservoir volume of at least 100 mL. FDA-approved product labeling provides detailed directions for the preparation of solutions with concentrations of 3,000 ng/mL, 5,000 ng/mL, 10,000 ng/mL, 15,000 ng/mL, and 30,000 ng/mL.[28168] [50003]

Storage: Protect from light. Refrigerate reconstituted solution at 2 to 8 degrees C (36 to 46 degrees F) if not used immediately.[28168] [50003] Stability and maximum administration times depend on the specific product and diluent used.

Flolan, when using Sterile Diluent for Flolan: When used at room temperature (15 to 25 degrees C [59 to 77 degrees F]), reconstituted solutions are stable for up to 8 hours after reconstitution or removal from refrigerated storage. May store for up to 40 hours refrigerated before use. When used with a cold pack, reconstituted solutions are stable for up to 24 hours. Change cold packs every 12 hours.

Refrigerated storage and infusion should not exceed 48 hours.[28168]

Flolan, when using pH 12 Sterile Diluent for Flolan: Reconstituted solutions, freshly prepared or stored refrigerated no longer than 8 days, can be administered up to 72 hours at up to 25 degrees C (77 degrees F), 48 hours at up to 30 degrees C (86 degrees F), 24 hours at up to 35 degrees C (95 degrees F), or 12 hours at up to 40 degrees C (104 degrees F).[28168]

Veletri:

For use at room temperature (25 degrees C [77 degrees F]): Reconstituted solutions with a concentration of 3,000 to less than 15,000 ng/mL are stable for 48 hours if used immediately and 24 hours if the solution was stored refrigerated; reconstituted solutions with a concentration of 15,000 to less than 60,000 ng/mL are stable for 48 hours if used immediately or if stored refrigerated; reconstituted solutions with a concentration of 60,000 ng/mL or more are stable for 72 hours if used immediately and 48 hours if the solution was stored refrigerated.

For use at temperatures 26 to 30 degrees C (78 to 86 degrees F): For solutions with a concentration less than 60,000 ng/mL, change the pump reservoir every 24 hours. For solution concentrations 60,000 ng/mL or more, a single reservoir may be administered up to 48 hours (immediately after reconstitution or after up to 8 days of refrigeration).

For use at temperatures 31 to 40 degrees C (87 to 104 degrees F): Solutions with a concentration of 60,000 ng/mL can be immediately administered for up to 24 hours.[50003]

Intravenous Infusion

Administer epoprostenol continuously via a central venous catheter using an ambulatory infusion pump. Temporary peripheral IV infusion may be used until central access is established.

The infusion pump used should be 1) small and lightweight, 2) be able to adjust infusion rates in 2 ng/kg/minute increments, 3) have alarms for occlusion, end of infusion, and low battery, 4) be accurate to +/- 6% of the programmed rate, and 5) be positive-pressure driven with intervals between pulses no more than 3 minutes apart. The reservoir should be made of polyvinyl chloride, polypropylene, or glass. Use a 60-inch microbore non-DEHP extension set with proximal antisiphon valve, low priming volume (0.9 mL), and in-line 0.22-micron filter. Patients should have access to a backup infusion pump to avoid interruptions in therapy. Do not administer with any other parenteral medications or solutions.[28168] [50003]

STORAGE

Generic:

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

Flolan:

- Discard unused portion. Do not store for later use.
- Protect from light
- Store between 68 to 77 degrees F, excursions permitted 59 to 86 degrees F
- Store in carton until time of use

Veletri:

- Discard unused portion. Do not store for later use.
- Protect from direct sunlight
- Store at controlled room temperature (between 68 and 77 degrees F)
- Store in carton

CONTRAINDICATIONS / PRECAUTIONS

Abrupt discontinuation

Abrupt discontinuation of epoprostenol therapy, including sudden reductions in dosage and interruptions in drug delivery may result in symptoms of rebound pulmonary hypertension. Symptoms can include dyspnea, dizziness and asthenia. One patient death was attributed to the interruption of epoprostenol therapy during clinical trials.

Hypotension

Since epoprostenol can cause hypotension, it should be used cautiously with other hypotensive drugs to avoid additive effects.

Heart failure

The chronic use of epoprostenol is relatively contraindicated in patients with CHF due to severe left ventricular systolic dysfunction. A large study intending to evaluate the use of epoprostenol in patients with NYHA class III and IV congestive heart failure was terminated after an analysis of 471 patients showed that patients receiving epoprostenol had a higher mortality rate than patients receiving standard therapy only.

Bleeding

Epoprostenol is a potent inhibitor of platelet aggregation. Therefore, an increased risk for hemorrhagic complications should be considered, particularly for patients with other risk factors for bleeding.

Pulmonary edema

Some patients with primary pulmonary hypertension have developed pulmonary edema during dose-ranging. Pulmonary edema in these patients may be associated with veno-occlusive disease. Epoprostenol should not be used chronically in patients who develop pulmonary edema during dose ranging.

Thromboembolic disease

Unless contraindicated, anticoagulant therapy should be administered to patients receiving epoprostenol to reduce the risk of thromboembolic disease, including pulmonary thromboembolism or systemic embolism through a patent foramen ovale.

Pregnancy

Pregnant women with untreated pulmonary arterial hypertension are at risk for heart failure, stroke, preterm delivery, and maternal and fetal death. Limited published data from case series and case reports have not established an association with epoprostenol and major birth defects, miscarriage or adverse maternal or fetal outcomes when epoprostenol is used during pregnancy. No evidence of impaired fertility or harm to the fetus have been observed at doses 2.5 times the recommended human dose in rats and 4.8 times the recommended human dose based on BSA in rabbits. It is not known if epoprostenol crosses the placenta; however, because it is rapidly hydrolyzed in the plasma after administration, it is unlikely that the fetus would be exposed to a clinically significant amount of drug. In addition, epoprostenol is a naturally-occurring prostaglandin in the fetus, and therefore, it is unlikely that maternal administration would result in direct adverse effects on the fetus or embryo. There is limited experience with the use of epoprostenol in the treatment of severe pre-eclampsia. Fetal bradycardia, fetal heart rate decelerations, and death were reported and were not attributed to the drug but rather to the severity of the disease in the mother. In addition, administration did not result in changes in maternal pulse, fetal pulse rate, or uterine contractility in a study of 13 women with either superimposed preeclampsia or preeclampsia. There was also no change in placental or fetal blood flow. Epoprostenol has also been used in pregnant women with pulmonary hypertension. One woman was successfully treated with both IV and inhaled epoprostenol with no adverse effects reported on the infant. In another case report, 3 women with pulmonary arterial hypertension received epoprostenol throughout their pregnancy and delivered with no adverse effects noted in the infants. The authors concluded that its use in stable patients may enable successful completion of pregnancy, but caution that pregnancy in women with pulmonary hypertension poses high risk to both the mother and child and should be avoided.

Breast-feeding

There are no data on the presence of epoprostenol in either human or animal milk, the effects on the breast-fed infant, or the effect on milk production. Consider the developmental and health benefits of breast-feeding along with the mother's clinical need for epoprostenol and any potential adverse effects on the breast-fed child from epoprostenol or the underlying maternal condition. However, because it is rapidly degraded at physiologic pH and probably in the gut, it is unlikely that a clinically significant amount of drug would be excreted into breast milk and available for exposure to a breast-feeding infant. In addition, inhaled epoprostenol has been administered directly to a premature neonate with beneficial effects. Consider the benefits of breast-feeding, the risk of potential infant exposure, and the risk of an untreated or inadequately treated condition. If a breast-feeding infant experiences an adverse effect related to a maternally ingested drug, health care providers are encouraged to report the adverse effect to the FDA.

ADVERSE REACTIONS

Severe

bradycardia / Rapid / 5.0-5.0
 heart failure / Delayed / Incidence not known
 pancytopenia / Delayed / Incidence not known
 pulmonary embolism / Delayed / Incidence not known
 hepatic failure / Delayed / Incidence not known
 pulmonary edema / Early / Incidence not known

Moderate

skin ulcer / Delayed / 39.0-39.0
 sinus tachycardia / Rapid / 1.0-35.0
 bleeding / Early / 11.0-19.0
 hypotension / Rapid / 13.0-16.0
 hyperesthesia / Delayed / 1.0-12.0
 chest pain (unspecified) / Early / 11.0-11.0
 dyspnea / Early / 2.0-2.0
 splenomegaly / Delayed / Incidence not known
 hyperthyroidism / Delayed / Incidence not known
 anemia / Delayed / Incidence not known

Mild

headache / Early / 46.0-83.0
 dizziness / Early / 8.0-83.0
 vomiting / Early / 32.0-67.0
 nausea / Early / 32.0-67.0
 anorexia / Delayed / 66.0-66.0
 flushing / Rapid / 23.0-58.0
 diarrhea / Early / 37.0-50.0
 myalgia / Early / 44.0-44.0
 musculoskeletal pain / Early / 3.0-35.0
 chills / Rapid / 25.0-25.0
 urticaria / Rapid / 25.0-25.0
 fever / Early / 25.0-25.0
 rash / Early / 25.0-25.0
 agitation / Early / 11.0-21.0
 anxiety / Delayed / 11.0-21.0
 tremor / Early / 21.0-21.0
 infection / Delayed / 18.0-18.0
 paresthesias / Delayed / 1.0-12.0
 abdominal pain / Early / 5.0-5.0
 back pain / Delayed / 2.0-2.0
 diaphoresis / Early / 1.0-1.0
 dyspepsia / Early / 1.0-1.0

DRUG INTERACTIONS

Acetabulol: (Moderate) Epoprostenol can have additive effects when administered with other antihypertensive agents, including beta-blockers. These effects can be used to therapeutic advantage, but dosage adjustments may be necessary.

Acetaminophen; Aspirin, ASA; Caffeine: (Moderate) When used concurrently with platelet inhibitors, epoprostenol may increase the risk of bleeding.

Acetaminophen; Chlorpheniramine; Dextromethorphan; Phenylephrine: (Major) Avoid use of sympathomimetic agents with epoprostenol. Sympathomimetics counteract the medications used to stabilize pulmonary hypertension, including epoprostenol. Sympathomimetics can increase blood pressure, increase heart rate, and may cause vasoconstriction resulting in chest pain and shortness of breath in these patients. Patients should be advised to avoid amphetamine drugs, decongestants (including nasal decongestants) and sympathomimetic anorexians for weight loss, including dietary supplements. Intravenous vasopressors may be used in the emergency management of pulmonary hypertension patients when needed, but hemodynamic monitoring and careful monitoring of cardiac status are needed to avoid ischemia and other complications.

Acetaminophen; Chlorpheniramine; Dextromethorphan; Pseudoephedrine: (Major) Avoid use of sympathomimetic agents with epoprostenol. Sympathomimetics counteract the medications used to stabilize pulmonary hypertension, including epoprostenol. Sympathomimetics can increase blood pressure, increase heart rate, and may cause vasoconstriction resulting in chest pain and shortness of breath in these patients. Patients should be advised to avoid amphetamine drugs, decongestants (including nasal decongestants) and sympathomimetic anorexians for weight loss, including dietary supplements. Intravenous vasopressors may be used in the emergency management of pulmonary hypertension patients when needed, but hemodynamic monitoring and careful monitoring of cardiac status are needed to avoid ischemia and other complications.

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Acetaminophen; Chlorpheniramine; Phenylephrine; Phenyltoloxamine: (Major) Avoid use of sympathomimetic agents with epoprostenol. Sympathomimetics counteract the medications used to stabilize pulmonary hypertension, including epoprostenol. Sympathomimetics can increase blood pressure, increase heart rate, and may cause vasoconstriction resulting in chest pain and shortness of breath in these patients. Patients should be advised to avoid amphetamine drugs, decongestants (including nasal decongestants) and sympathomimetic anorexians for weight loss, including dietary supplements. Intravenous vasopressors may be used in the emergency management of pulmonary hypertension patients when needed, but hemodynamic monitoring and careful monitoring of cardiac status are needed to avoid ischemia and other complications.

Acetaminophen; Dextromethorphan; Guaifenesin; Phenylephrine: (Major) Avoid use of sympathomimetic agents with epoprostenol. Sympathomimetics counteract the medications used to stabilize pulmonary hypertension, including epoprostenol. Sympathomimetics can increase blood pressure, increase heart rate, and may cause vasoconstriction resulting in chest pain and shortness of breath in these patients. Patients should be advised to avoid amphetamine drugs, decongestants (including nasal decongestants) and sympathomimetic anorexians for weight loss, including dietary supplements. Intravenous vasopressors may be used in the emergency management of pulmonary hypertension patients when needed, but hemodynamic monitoring and careful monitoring of cardiac status are needed to avoid ischemia and other complications.

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Acetaminophen; Dichloralphenazone; Isometheptene: (Major) Avoid use of sympathomimetic agents with epoprostenol. Sympathomimetics counteract the medications used to stabilize pulmonary hypertension, including epoprostenol. Sympathomimetics can increase blood pressure, increase heart rate, and may cause vasoconstriction resulting in chest pain and shortness of breath in these patients. Patients should be advised to avoid amphetamine drugs, decongestants (including nasal decongestants) and sympathomimetic anorexians for weight loss, including dietary supplements. Intravenous vasopressors may be used in the emergency management of pulmonary hypertension patients when needed, but hemodynamic monitoring and careful monitoring of cardiac status are needed to avoid ischemia and other complications.

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Acetazolamide: (Moderate) Further reductions in blood pressure may occur when epoprostenol is administered with other antihypertensive agents.

Acrivastine; Pseudoephedrine: (Major) Avoid use of sympathomimetic agents with epoprostenol. Sympathomimetics counteract the medications used to stabilize pulmonary hypertension, including epoprostenol. Sympathomimetics can increase blood pressure, increase heart rate, and may cause vasoconstriction resulting in chest pain and shortness of breath in these patients. Patients should be advised to avoid amphetamine drugs, decongestants (including nasal decongestants) and sympathomimetic anorexians for weight loss, including dietary supplements. Intravenous vasopressors may be used in the emergency management of pulmonary hypertension patients when needed, but hemodynamic monitoring and careful monitoring of cardiac status are needed to avoid ischemia and other complications.

Aldesleukin, IL-2: (Moderate) Epoprostenol may potentiate the hypotension seen with aldesleukin, IL 2.

Alemtuzumab: (Moderate) Alemtuzumab may cause hypotension. Careful monitoring of blood pressure and hypotensive symptoms is recommended especially in patients with ischemic heart disease and in patients on antihypertensive agents.

Aliskiren: (Moderate) Aliskiren can enhance the effects of epoprostenol on blood pressure if given concomitantly. This additive effect may be desirable, but dosages must be adjusted accordingly. Blood pressure and electrolytes should be routinely monitored in patients receiving aliskiren.

Aliskiren; Amlodipine: (Moderate) Aliskiren can enhance the effects of epoprostenol on blood pressure if given concomitantly. This additive effect may be desirable, but dosages must be adjusted accordingly. Blood pressure and electrolytes should be routinely monitored in patients receiving aliskiren. (Moderate) Calcium-channel blockers can have additive hypotensive effects with other antihypertensive agents. This additive effect can be desirable, but the patient should be monitored carefully and the dosage should be adjusted based on clinical response.

Aliskiren; Amlodipine; Hydrochlorothiazide, HCTZ: (Moderate) Aliskiren can enhance the effects of epoprostenol on blood pressure if given concomitantly. This additive effect may be desirable, but dosages must be adjusted accordingly. Blood pressure and electrolytes should be routinely monitored in patients receiving aliskiren. (Moderate) Calcium-channel blockers can have additive hypotensive effects with other antihypertensive agents. This additive effect can be desirable, but the patient should be monitored carefully and the dosage should be adjusted based on clinical response.

Aliskiren; Hydrochlorothiazide, HCTZ: (Moderate) Aliskiren can enhance the effects of epoprostenol on blood pressure if given concomitantly. This additive effect may be desirable, but dosages must be adjusted accordingly. Blood pressure and electrolytes should be routinely monitored in patients receiving aliskiren.

Aliskiren; Valsartan: (Moderate) Aliskiren can enhance the effects of epoprostenol on blood pressure if given concomitantly. This additive effect may be desirable, but dosages must be adjusted accordingly. Blood pressure and electrolytes should be routinely monitored in patients receiving aliskiren. (Moderate) Angiotensin II receptor antagonists can enhance the hypotensive effects of antihypertensive agents if given concomitantly. This additive effect may be desirable, but dosages must be adjusted accordingly.

Alpha-blockers: (Minor) Epoprostenol can have additive effects when administered with other antihypertensive agents, including alpha-blockers. These effects can be used to therapeutic advantage, but dosage adjustments may be necessary.

Alprostadil: (Minor) Systemic alprostadil and epoprostenol are both prostaglandins that reduce blood pressure, and would not be commonly prescribed together at the same time. The concomitant use of systemic alprostadil injection and epoprostenol would be expected to cause additive hypotension. Systemic drug interactions with the urethral suppository (MUSE) or alprostadil intracavernous injection are unlikely in most patients because low or undetectable amounts of the drug are found in the peripheral venous circulation following administration. In those men with significant corpora cavernosa venous leakage, hypotension might be more likely. Use caution with in-clinic dosing for erectile dysfunction (ED) and monitor for the effects on blood pressure. However, in clinical trials with alprostadil intracavernous injection, anti-hypertensive agents had no apparent effect on the safety and efficacy of alprostadil.

Ambrisentan: (Moderate) Although no specific interactions have been documented, ambrisentan has vasodilatory effects and may contribute additive hypotensive effects when given with other antihypertensive agents. Patients receiving ambrisentan in combination with other antihypertensive agents should be monitored for decreases in blood pressure.

Amifostine: (Major) Patients receiving antihypertensive agents should be closely monitored during amifostine infusions due to additive effects. If possible, patients should not take their antihypertensive medication 24 hours before receiving amifostine. Patients who can not stop their antihypertensive agents should not receive amifostine or be closely monitored during the infusion and, possibly, given lower doses.

Amlodipine: (Moderate) Calcium-channel blockers can have additive hypotensive effects with other antihypertensive agents. This additive effect can be desirable, but the patient should be monitored carefully and the dosage should be adjusted based on clinical response.

Amlodipine; Atorvastatin: (Moderate) Calcium-channel blockers can have additive hypotensive effects with other antihypertensive agents. This additive effect can be desirable, but the patient should be monitored carefully and the dosage should be adjusted based on clinical response.

Amlodipine; Benazepril: (Moderate) Calcium-channel blockers can have additive hypotensive effects with other antihypertensive agents. This additive effect can be desirable, but the patient should be monitored carefully and the dosage should be adjusted based on clinical response.

Amlodipine; Celecoxib: (Moderate) Calcium-channel blockers can have additive hypotensive effects with other antihypertensive agents. This additive effect can be desirable, but the patient should be monitored carefully and the dosage should be adjusted based on clinical response.

(Moderate) NSAIDs may decrease the effect of antihypertensive agents through various mechanisms, including renal and peripheral vasoactive pathways.

Amlodipine; Olmesartan: (Moderate) Angiotensin II receptor antagonists can enhance the hypotensive effects of antihypertensive agents if given concomitantly. This additive effect may be desirable, but dosages must be adjusted accordingly. (Moderate) Calcium-channel blockers can have additive hypotensive effects with other antihypertensive agents. This additive effect can be desirable, but the patient should be monitored carefully and the dosage should be adjusted based on clinical response.

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Amlodipine; Valsartan; Hydrochlorothiazide, HCTZ: (Moderate) Angiotensin II receptor antagonists can enhance the hypotensive effects of antihypertensive agents if given concomitantly. This additive effect may be desirable, but dosages must be adjusted accordingly. (Moderate) Calcium-channel blockers can have additive hypotensive effects with other antihypertensive agents. This additive effect can be desirable, but the patient should be monitored carefully and the dosage should be adjusted based on clinical response.

Amobarbital: (Moderate) Concurrent use of amobarbital with antihypertensive agents may lead to hypotension. Monitor for decreases in blood pressure during times of coadministration.

Amphetamine: (Major) Avoid use of sympathomimetic agents with epoprostenol. Sympathomimetics counteract the medications used to stabilize pulmonary hypertension, including epoprostenol. Sympathomimetics can increase blood pressure, increase heart rate, and may cause vasoconstriction resulting in chest pain and shortness of breath in these patients. Patients should be advised to avoid amphetamine drugs, decongestants (including nasal decongestants) and sympathomimetic anorexiant for weight loss, including dietary supplements. Intravenous vasopressors may be used in the emergency management of pulmonary hypertension patients when needed, but hemodynamic monitoring and careful monitoring of cardiac status are needed to avoid ischemia and other complications.

Amphetamine; Dextroamphetamine: (Major) Avoid use of sympathomimetic agents with epoprostenol. Sympathomimetics counteract the medications used to stabilize pulmonary hypertension, including epoprostenol. Sympathomimetics can increase blood pressure, increase heart rate, and may cause vasoconstriction resulting in chest pain and shortness of breath in these patients. Patients should be advised to avoid amphetamine drugs, decongestants (including nasal decongestants) and sympathomimetic anorexiant for weight loss, including dietary supplements. Intravenous vasopressors may be used in the emergency management of pulmonary hypertension patients when needed, but hemodynamic monitoring and careful monitoring of cardiac status are needed to avoid ischemia and other complications.

Amyl Nitrite: (Moderate) Concomitant use of nitrates with other antihypertensive agents can cause additive hypotensive effects. Dosage adjustments may be necessary.

Angiotensin II receptor antagonists: (Moderate) Angiotensin II receptor antagonists can enhance the hypotensive effects of antihypertensive agents if given concomitantly. This additive effect may be desirable, but dosages must be adjusted accordingly.

Anticoagulants: (Moderate) When used concurrently with anticoagulants, epoprostenol may increase the risk of bleeding.

Antithrombin III: (Moderate) When used concurrently with anticoagulants, epoprostenol may increase the risk of bleeding.

Apixaban: (Moderate) When used concurrently with anticoagulants, epoprostenol may increase the risk of bleeding.

Apraclonidine: (Minor) Alpha blockers as a class may reduce heart rate and blood pressure. While no specific drug interactions have been identified with systemic agents and apraclonidine during clinical trials, it is theoretically possible that additive blood pressure reductions could occur when apraclonidine is combined with the use of antihypertensive agents. Patients using cardiovascular drugs concomitantly with apraclonidine should have their pulse and blood pressure monitored periodically.

Argatroban: (Moderate) When used concurrently with anticoagulants, epoprostenol may increase the risk of bleeding.

Aripiprazole: (Minor) Aripiprazole may enhance the hypotensive effects of antihypertensive agents.

Articaine; Epinephrine: (Major) Avoid use of sympathomimetic agents with epoprostenol. Sympathomimetics counteract the medications used to stabilize pulmonary hypertension, including epoprostenol. Sympathomimetics can increase blood pressure, increase heart rate, and may cause vasoconstriction resulting in chest pain and shortness of breath in these patients. Patients should be advised to avoid amphetamine drugs, decongestants (including nasal decongestants) and sympathomimetic anorexiant for weight loss, including dietary supplements. Intravenous vasopressors may be used in the emergency management of pulmonary hypertension patients when needed, but hemodynamic monitoring and careful monitoring of cardiac status are needed to avoid ischemia and other complications.

Asenapine: (Moderate) Secondary to alpha-blockade, asenapine can produce vasodilation that may result in additive effects during concurrent use of antihypertensive agents. The potential reduction in blood pressure can precipitate orthostatic hypotension and associated dizziness, tachycardia, and syncope. If concurrent use of asenapine and antihypertensive agents is necessary, patients should be counseled on measures to prevent orthostatic hypotension, such as sitting on the edge of the bed for several minutes prior to standing in the morning and rising slowly from a seated position. Close monitoring of blood pressure is recommended until the full effects of the combination therapy are known.

Aspirin, ASA: (Moderate) When used concurrently with platelet inhibitors, epoprostenol may increase the risk of bleeding.

Aspirin, ASA; Butalbital; Caffeine: (Moderate) When used concurrently with platelet inhibitors, epoprostenol may increase the risk of bleeding.

Aspirin, ASA; Butalbital; Caffeine; Codeine: (Moderate) When used concurrently with platelet inhibitors, epoprostenol may increase the risk of bleeding.

Aspirin, ASA; Caffeine: (Moderate) When used concurrently with platelet inhibitors, epoprostenol may increase the risk of bleeding.

Aspirin, ASA; Caffeine; Dihydrocodeine: (Moderate) When used concurrently with platelet inhibitors, epoprostenol may increase the risk of bleeding.

Aspirin, ASA; Caffeine; Orphenadrine: (Moderate) When used concurrently with platelet inhibitors, epoprostenol may increase the risk of bleeding.

Aspirin, ASA; Carisoprodol: (Moderate) When used concurrently with platelet inhibitors, epoprostenol may increase the risk of bleeding.

Aspirin, ASA; Carisoprodol; Codeine: (Moderate) When used concurrently with platelet inhibitors, epoprostenol may increase the risk of bleeding.

Aspirin, ASA; Citric Acid; Sodium Bicarbonate: (Moderate) When used concurrently with platelet inhibitors, epoprostenol may increase the risk of bleeding.

Aspirin, ASA; Dipyridamole: (Moderate) When used concurrently with platelet inhibitors, epoprostenol may increase the risk of bleeding.

Aspirin, ASA; Omeprazole: (Moderate) When used concurrently with platelet inhibitors, epoprostenol may increase the risk of bleeding.

Aspirin, ASA; Oxycodone: (Moderate) When used concurrently with platelet inhibitors, epoprostenol may increase the risk of bleeding.

Aspirin, ASA; Pravastatin: (Moderate) When used concurrently with platelet inhibitors, epoprostenol may increase the risk of bleeding.

Atenolol: (Moderate) Epoprostenol can have additive effects when administered with other antihypertensive agents, including beta-blockers. These effects can be used to therapeutic advantage, but dosage adjustments may be necessary.

Atenolol; Chlorthalidone: (Moderate) Epoprostenol can have additive effects when administered with other antihypertensive agents, including beta-blockers. These effects can be used to therapeutic advantage, but dosage adjustments may be necessary.

Azilsartan: (Moderate) Angiotensin II receptor antagonists can enhance the hypotensive effects of antihypertensive agents if given concomitantly. This additive effect may be desirable, but dosages must be adjusted accordingly.

Azilsartan; Chlorthalidone: (Moderate) Angiotensin II receptor antagonists can enhance the hypotensive effects of antihypertensive agents if given concomitantly. This additive effect may be desirable, but dosages must be adjusted accordingly.

Baclofen: (Moderate) Baclofen has been associated with hypotension. Concurrent use with baclofen and antihypertensive agents may result in additive hypotension. Dosage adjustments of the antihypertensive medication may be required.

Bendroflumethiazide; Nadolol: (Moderate) Epoprostenol can have additive effects when administered with other antihypertensive agents, including beta-blockers. These effects can be used to therapeutic advantage, but dosage adjustments may be necessary.

Benzphetamine: (Major) Avoid use of sympathomimetic agents with epoprostenol. Sympathomimetics counteract the medications used to stabilize pulmonary hypertension, including epoprostenol. Sympathomimetics can increase blood pressure, increase heart rate, and may cause vasoconstriction resulting in chest pain and shortness of breath in these patients. Patients should be advised to avoid amphetamine drugs, decongestants (including nasal decongestants) and sympathomimetic anorexiant for weight loss, including dietary supplements. Intravenous vasopressors may be used in the emergency management of pulmonary hypertension patients when needed, but hemodynamic monitoring and careful monitoring of cardiac status are needed to avoid ischemia and other complications.

Beta-blockers: (Moderate) Epoprostenol can have additive effects when administered with other antihypertensive agents, including beta-blockers. These effects can be used to therapeutic advantage, but dosage adjustments may be necessary.

Betaxolol: (Moderate) Epoprostenol can have additive effects when administered with other antihypertensive agents, including beta-blockers. These effects can be used to therapeutic advantage, but dosage adjustments may be necessary.

Betrixaban: (Moderate) When used concurrently with anticoagulants, epoprostenol may increase the risk of bleeding.

Bisoprolol: (Moderate) Epoprostenol can have additive effects when administered with other antihypertensive agents, including beta-blockers. These effects can be used to therapeutic advantage, but dosage adjustments may be necessary.

Bisoprolol; Hydrochlorothiazide, HCTZ: (Moderate) Epoprostenol can have additive effects when administered with other antihypertensive agents, including beta-blockers. These effects can be used to therapeutic advantage, but dosage adjustments may be necessary.

Bivalirudin: (Moderate) When used concurrently with anticoagulants, epoprostenol may increase the risk of bleeding.

Bortezomib: (Moderate) Patients on antihypertensive agents receiving bortezomib treatment may require close monitoring of their blood pressure and dosage adjustment of their medication. During clinical trials of bortezomib, hypotension was reported in roughly 12 percent of patients.

Brimonidine; Timolol: (Moderate) Epoprostenol can have additive effects when administered with other antihypertensive agents, including beta-blockers. These effects can be used to therapeutic advantage, but dosage adjustments may be necessary.

Brompheniramine; Carbetapentane; Phenylephrine: (Major) Avoid use of sympathomimetic agents with epoprostenol. Sympathomimetics counteract the medications used to stabilize pulmonary hypertension, including epoprostenol. Sympathomimetics can increase blood pressure, increase heart rate, and may cause vasoconstriction resulting in chest pain and shortness of breath in these patients. Patients should be advised to avoid amphetamine drugs, decongestants (including nasal decongestants) and sympathomimetic anorexiant for weight loss, including dietary supplements. Intravenous vasopressors may be used in the emergency management of pulmonary hypertension patients when needed, but hemodynamic monitoring and careful monitoring of cardiac status are needed to avoid ischemia and other complications.

Brompheniramine; Dextromethorphan; Phenylephrine: (Major) Avoid use of sympathomimetic agents with epoprostenol. Sympathomimetics counteract the medications used to stabilize pulmonary hypertension, including epoprostenol. Sympathomimetics can increase blood pressure, increase heart rate, and may cause vasoconstriction resulting in chest pain and shortness of breath in these patients. Patients should be advised to avoid amphetamine drugs, decongestants (including nasal decongestants) and sympathomimetic anorexiant for weight loss, including dietary supplements. Intravenous vasopressors may be used in the emergency management of pulmonary hypertension patients when needed, but hemodynamic monitoring and careful monitoring of cardiac status are needed to avoid ischemia and other complications.

Brompheniramine; Hydrocodone; Pseudoephedrine: (Major) Avoid use of sympathomimetic agents with epoprostenol. Sympathomimetics counteract the medications used to stabilize pulmonary hypertension, including epoprostenol. Sympathomimetics can increase blood pressure, increase heart rate, and may cause vasoconstriction resulting in chest pain and shortness of breath in these patients. Patients should be advised to avoid amphetamine drugs, decongestants (including nasal decongestants) and sympathomimetic anorexiant for weight loss, including dietary supplements. Intravenous vasopressors may be used in the emergency management of pulmonary hypertension patients when needed, but hemodynamic monitoring and careful monitoring of cardiac status are needed to avoid ischemia and other complications.

Brompheniramine; Phenylephrine: (Major) Avoid use of sympathomimetic agents with epoprostenol. Sympathomimetics counteract the medications used to stabilize pulmonary hypertension, including epoprostenol. Sympathomimetics can increase blood pressure, increase heart rate, and may cause vasoconstriction resulting in chest pain and shortness of breath in these patients. Patients should be advised to avoid amphetamine drugs, decongestants (including nasal decongestants) and sympathomimetic anorexiant for weight loss, including dietary supplements. Intravenous vasopressors may be used in the emergency management of pulmonary hypertension patients when needed, but hemodynamic monitoring and careful monitoring of cardiac status are needed to avoid ischemia and other complications.

Brompheniramine; Pseudoephedrine: (Major) Avoid use of sympathomimetic agents with epoprostenol. Sympathomimetics counteract the medications used to stabilize pulmonary hypertension, including epoprostenol. Sympathomimetics can increase blood pressure, increase heart rate, and may cause vasoconstriction resulting in chest pain and shortness of breath in these patients. Patients should be advised to avoid amphetamine drugs, decongestants (including nasal decongestants) and sympathomimetic anorexiant for weight loss, including dietary supplements. Intravenous vasopressors may be used in the emergency management of pulmonary hypertension patients when needed, but hemodynamic monitoring and careful monitoring of cardiac status are needed to avoid ischemia and other complications.

Brompheniramine; Pseudoephedrine; Dextromethorphan: (Major) Avoid use of sympathomimetic agents with epoprostenol. Sympathomimetics counteract the medications used to stabilize pulmonary hypertension, including epoprostenol. Sympathomimetics can increase blood pressure, increase heart rate, and may cause vasoconstriction resulting in chest pain and shortness of breath in these patients. Patients should be advised to avoid amphetamine drugs, decongestants (including nasal decongestants) and sympathomimetic anorexiant for weight loss, including dietary supplements. Intravenous vasopressors may be used in the emergency management of pulmonary hypertension patients when needed, but hemodynamic monitoring and careful monitoring of cardiac status are needed to avoid ischemia and other complications.

Bupivacaine; Meloxicam: (Moderate) NSAIDs may decrease the effect of antihypertensive agents through various mechanisms, including renal and peripheral vasoactive pathways.

Calcium-channel blockers: (Moderate) Calcium-channel blockers can have additive hypotensive effects with other antihypertensive agents. This additive effect can be desirable, but the patient should be monitored carefully and the dosage should be adjusted based on clinical response.

Candesartan: (Moderate) Angiotensin II receptor antagonists can enhance the hypotensive effects of antihypertensive agents if given concomitantly. This additive effect may be desirable, but dosages must be adjusted accordingly.

Candesartan; Hydrochlorothiazide, HCTZ: (Moderate) Angiotensin II receptor antagonists can enhance the hypotensive effects of antihypertensive agents if given concomitantly. This additive effect may be desirable, but dosages must be adjusted accordingly.

Carbetapentane; Chlorpheniramine; Phenylephrine: (Major) Avoid use of sympathomimetic agents with epoprostenol. Sympathomimetics counteract the medications used to stabilize pulmonary hypertension, including epoprostenol. Sympathomimetics can increase blood pressure, increase heart rate, and may cause vasoconstriction resulting in chest pain and shortness of breath in these patients. Patients should be advised to avoid amphetamine drugs, decongestants (including nasal decongestants) and sympathomimetic anorexiant for weight loss, including dietary supplements. Intravenous vasopressors may be used in the emergency management of pulmonary hypertension patients when needed, but hemodynamic monitoring and careful monitoring of cardiac status are needed to avoid ischemia and other complications.

Carbetapentane; Diphenhydramine; Phenylephrine: (Major) Avoid use of sympathomimetic agents with epoprostenol. Sympathomimetics counteract the medications used to stabilize pulmonary hypertension, including epoprostenol. Sympathomimetics can increase blood pressure, increase heart rate, and may cause vasoconstriction resulting in chest pain and shortness of breath in these patients. Patients should be advised to avoid amphetamine drugs, decongestants (including nasal decongestants) and sympathomimetic anorexiant for weight loss, including dietary supplements. Intravenous vasopressors may be used in the emergency management of pulmonary hypertension patients when needed, but hemodynamic monitoring and careful monitoring of cardiac status are needed to avoid ischemia and other complications.

Carbetapentane; Guaifenesin; Phenylephrine: (Major) Avoid use of sympathomimetic agents with epoprostenol. Sympathomimetics counteract the medications used to stabilize pulmonary hypertension, including epoprostenol. Sympathomimetics can increase blood pressure, increase heart rate, and may cause vasoconstriction resulting in chest pain and shortness of breath in these patients. Patients should be advised to avoid amphetamine drugs, decongestants (including nasal decongestants) and sympathomimetic anorexiant for weight loss, including dietary supplements. Intravenous vasopressors may be used in the emergency management of pulmonary hypertension patients when needed, but hemodynamic monitoring and careful monitoring of cardiac status are needed to avoid ischemia and other complications.

Carbetapentane; Phenylephrine: (Major) Avoid use of sympathomimetic agents with epoprostenol. Sympathomimetics counteract the medications used to stabilize pulmonary hypertension, including epoprostenol. Sympathomimetics can increase blood pressure, increase heart rate, and may cause vasoconstriction resulting in chest pain and shortness of breath in these patients. Patients should be advised to avoid amphetamine drugs, decongestants (including nasal decongestants) and sympathomimetic anorexiant for weight loss, including dietary supplements. Intravenous vasopressors may be used in the emergency management of pulmonary hypertension patients when needed, but hemodynamic monitoring and careful monitoring of cardiac status are needed to avoid ischemia and other complications.

Carbetapentane; Phenylephrine; Pyrilamine: (Major) Avoid use of sympathomimetic agents with epoprostenol. Sympathomimetics counteract the medications used to stabilize pulmonary hypertension, including epoprostenol. Sympathomimetics can increase blood pressure, increase heart rate, and may cause vasoconstriction resulting in chest pain and shortness of breath in these patients. Patients should be advised to avoid amphetamine drugs, decongestants (including nasal decongestants) and sympathomimetic anorexiant for weight loss, including dietary supplements. Intravenous vasopressors may be used in the emergency management of pulmonary hypertension patients when needed, but hemodynamic monitoring and careful monitoring of cardiac status are needed to avoid ischemia and other complications.

Carbetapentane; Pseudoephedrine: (Major) Avoid use of sympathomimetic agents with epoprostenol. Sympathomimetics counteract the medications used to stabilize pulmonary hypertension, including epoprostenol. Sympathomimetics can increase blood pressure, increase heart

rate, and may cause vasoconstriction resulting in chest pain and shortness of breath in these patients. Patients should be advised to avoid amphetamine drugs, decongestants (including nasal decongestants) and sympathomimetic anorexiant for weight loss, including dietary supplements. Intravenous vasopressors may be used in the emergency management of pulmonary hypertension patients when needed, but hemodynamic monitoring and careful monitoring of cardiac status are needed to avoid ischemia and other complications.

Carbidopa; Levodopa: (Moderate) Concomitant use of antihypertensive agents with levodopa can result in additive hypotensive effects.

Carbidopa; Levodopa; Entacapone: (Moderate) Concomitant use of antihypertensive agents with levodopa can result in additive hypotensive effects.

Carbinoxamine; Dextromethorphan; Pseudoephedrine: (Major) Avoid use of sympathomimetic agents with epoprostenol. Sympathomimetics counteract the medications used to stabilize pulmonary hypertension, including epoprostenol. Sympathomimetics can increase blood pressure, increase heart rate, and may cause vasoconstriction resulting in chest pain and shortness of breath in these patients. Patients should be advised to avoid amphetamine drugs, decongestants (including nasal decongestants) and sympathomimetic anorexiant for weight loss, including dietary supplements. Intravenous vasopressors may be used in the emergency management of pulmonary hypertension patients when needed, but hemodynamic monitoring and careful monitoring of cardiac status are needed to avoid ischemia and other complications.

Carbinoxamine; Hydrocodone; Phenylephrine: (Major) Avoid use of sympathomimetic agents with epoprostenol. Sympathomimetics counteract the medications used to stabilize pulmonary hypertension, including epoprostenol. Sympathomimetics can increase blood pressure, increase heart rate, and may cause vasoconstriction resulting in chest pain and shortness of breath in these patients. Patients should be advised to avoid amphetamine drugs, decongestants (including nasal decongestants) and sympathomimetic anorexiant for weight loss, including dietary supplements. Intravenous vasopressors may be used in the emergency management of pulmonary hypertension patients when needed, but hemodynamic monitoring and careful monitoring of cardiac status are needed to avoid ischemia and other complications.

Carbinoxamine; Hydrocodone; Pseudoephedrine: (Major) Avoid use of sympathomimetic agents with epoprostenol. Sympathomimetics counteract the medications used to stabilize pulmonary hypertension, including epoprostenol. Sympathomimetics can increase blood pressure, increase heart rate, and may cause vasoconstriction resulting in chest pain and shortness of breath in these patients. Patients should be advised to avoid amphetamine drugs, decongestants (including nasal decongestants) and sympathomimetic anorexiant for weight loss, including dietary supplements. Intravenous vasopressors may be used in the emergency management of pulmonary hypertension patients when needed, but hemodynamic monitoring and careful monitoring of cardiac status are needed to avoid ischemia and other complications.

Carbinoxamine; Phenylephrine: (Major) Avoid use of sympathomimetic agents with epoprostenol. Sympathomimetics counteract the medications used to stabilize pulmonary hypertension, including epoprostenol. Sympathomimetics can increase blood pressure, increase heart rate, and may cause vasoconstriction resulting in chest pain and shortness of breath in these patients. Patients should be advised to avoid amphetamine drugs, decongestants (including nasal decongestants) and sympathomimetic anorexiant for weight loss, including dietary supplements. Intravenous vasopressors may be used in the emergency management of pulmonary hypertension patients when needed, but hemodynamic monitoring and careful monitoring of cardiac status are needed to avoid ischemia and other complications.

Carbinoxamine; Pseudoephedrine: (Major) Avoid use of sympathomimetic agents with epoprostenol. Sympathomimetics counteract the medications used to stabilize pulmonary hypertension, including epoprostenol. Sympathomimetics can increase blood pressure, increase heart rate, and may cause vasoconstriction resulting in chest pain and shortness of breath in these patients. Patients should be advised to avoid amphetamine drugs, decongestants (including nasal decongestants) and sympathomimetic anorexiant for weight loss, including dietary supplements. Intravenous vasopressors may be used in the emergency management of pulmonary hypertension patients when needed, but hemodynamic monitoring and careful monitoring of cardiac status are needed to avoid ischemia and other complications.

Carbonic anhydrase inhibitors: (Moderate) Further reductions in blood pressure may occur when epoprostenol is administered with other antihypertensive agents.

Cariprazine: (Moderate) Orthostatic vital signs should be monitored in patients who are at risk for hypotension, such as those receiving cariprazine in combination with antihypertensive agents. Atypical antipsychotics may cause orthostatic hypotension and syncope, most commonly during treatment initiation and dosage increases. Patients should be informed about measures to prevent orthostatic hypotension, such as sitting on the edge of the bed for several minutes prior to standing in the morning, or rising slowly from a seated position. Consider a cariprazine dose reduction if hypotension occurs.

Carteolol: (Moderate) Epoprostenol can have additive effects when administered with other antihypertensive agents, including beta-blockers. These effects can be used to therapeutic advantage, but dosage adjustments may be necessary.

Carvedilol: (Moderate) Epoprostenol can have additive effects when administered with other antihypertensive agents, including beta-blockers. These effects can be used to therapeutic advantage, but dosage adjustments may be necessary.

Celecoxib: (Moderate) NSAIDs may decrease the effect of antihypertensive agents through various mechanisms, including renal and peripheral vasoactive pathways.

Central-acting adrenergic agents: (Moderate) The concomitant administration of epoprostenol with other antihypertensive agents can result in additive hypotensive effects. This can be therapeutically advantageous, but dosages must be adjusted accordingly.

Cetirizine; Pseudoephedrine: (Major) Avoid use of sympathomimetic agents with epoprostenol. Sympathomimetics counteract the medications used to stabilize pulmonary hypertension, including epoprostenol. Sympathomimetics can increase blood pressure, increase heart rate, and may cause vasoconstriction resulting in chest pain and shortness of breath in these patients. Patients should be advised to avoid amphetamine drugs, decongestants (including nasal decongestants) and sympathomimetic anorexiant for weight loss, including dietary supplements. Intravenous vasopressors may be used in the emergency management of pulmonary hypertension patients when needed, but hemodynamic monitoring and careful monitoring of cardiac status are needed to avoid ischemia and other complications.

Chlophedianol; Dexchlorpheniramine; Pseudoephedrine: (Major) Avoid use of sympathomimetic agents with epoprostenol. Sympathomimetics counteract the medications used to stabilize pulmonary hypertension, including epoprostenol. Sympathomimetics can increase blood pressure, increase heart rate, and may cause vasoconstriction resulting in chest pain and shortness of breath in these patients. Patients should be advised to avoid amphetamine drugs, decongestants (including nasal decongestants) and sympathomimetic anorexiant for weight loss, including dietary supplements. Intravenous vasopressors may be used in the emergency management of pulmonary hypertension patients when needed, but hemodynamic monitoring and careful monitoring of cardiac status are needed to avoid ischemia and other complications.

Chlophedianol; Guaifenesin; Phenylephrine: (Major) Avoid use of sympathomimetic agents with epoprostenol. Sympathomimetics counteract the medications used to stabilize pulmonary hypertension, including epoprostenol. Sympathomimetics can increase blood pressure, increase heart rate, and may cause vasoconstriction resulting in chest pain and shortness of breath in these patients. Patients should be advised to avoid amphetamine drugs, decongestants (including nasal decongestants) and sympathomimetic anorexiant for weight loss, including dietary supplements. Intravenous vasopressors may be used in the emergency management of pulmonary hypertension patients when needed, but hemodynamic monitoring and careful monitoring of cardiac status are needed to avoid ischemia and other complications.

Chlorpheniramine; Dextromethorphan; Phenylephrine: (Major) Avoid use of sympathomimetic agents with epoprostenol. Sympathomimetics counteract the medications used to stabilize pulmonary hypertension, including epoprostenol. Sympathomimetics can increase blood pressure, increase heart rate, and may cause vasoconstriction resulting in chest pain and shortness of breath in these patients. Patients should be advised to avoid amphetamine drugs, decongestants (including nasal decongestants) and sympathomimetic anorexiant for weight loss, including dietary supplements. Intravenous vasopressors may be used in the emergency management of pulmonary hypertension patients when needed, but hemodynamic monitoring and careful monitoring of cardiac status are needed to avoid ischemia and other complications.

Chlorpheniramine; Dextromethorphan; Pseudoephedrine: (Major) Avoid use of sympathomimetic agents with epoprostenol. Sympathomimetics counteract the medications used to stabilize pulmonary hypertension, including epoprostenol. Sympathomimetics can increase blood pressure, increase heart rate, and may cause vasoconstriction resulting in chest pain and shortness of breath in these patients. Patients should be advised to avoid amphetamine drugs, decongestants (including nasal decongestants) and sympathomimetic anorexiant for weight loss, including dietary supplements. Intravenous vasopressors may be used in the emergency management of pulmonary hypertension patients when needed, but hemodynamic monitoring and careful monitoring of cardiac status are needed to avoid ischemia and other complications.

Chlorpheniramine; Dihydrocodeine; Phenylephrine: (Major) Avoid use of sympathomimetic agents with epoprostenol. Sympathomimetics counteract the medications used to stabilize pulmonary hypertension, including epoprostenol. Sympathomimetics can increase blood pressure, increase heart rate, and may cause vasoconstriction resulting in chest pain and shortness of breath in these patients. Patients should be advised to avoid amphetamine drugs, decongestants (including nasal decongestants) and sympathomimetic anorexiant for weight loss, including dietary supplements. Intravenous vasopressors may be used in the emergency management of pulmonary hypertension patients when needed, but hemodynamic monitoring and careful monitoring of cardiac status are needed to avoid ischemia and other complications.

Chlorpheniramine; Dihydrocodeine; Pseudoephedrine: (Major) Avoid use of sympathomimetic agents with epoprostenol. Sympathomimetics counteract the medications used to stabilize pulmonary hypertension, including epoprostenol. Sympathomimetics can increase blood pressure, increase heart rate, and may cause vasoconstriction resulting in chest pain and shortness of breath in these patients. Patients should be advised to avoid amphetamine drugs, decongestants (including nasal decongestants) and sympathomimetic anorexiant for weight loss, including dietary supplements. Intravenous vasopressors may be used in the emergency management of pulmonary hypertension patients when needed, but hemodynamic monitoring and careful monitoring of cardiac status are needed to avoid ischemia and other complications.

Chlorpheniramine; Guaifenesin; Hydrocodone; Pseudoephedrine: (Major) Avoid use of sympathomimetic agents with epoprostenol. Sympathomimetics counteract the medications used to stabilize pulmonary hypertension, including epoprostenol. Sympathomimetics can increase blood pressure, increase heart rate, and may cause vasoconstriction resulting in chest pain and shortness of breath in these patients. Patients should be advised to avoid amphetamine drugs, decongestants (including nasal decongestants) and sympathomimetic anorexiant for weight loss, including dietary supplements. Intravenous vasopressors may be used in the emergency management of pulmonary hypertension patients when needed, but hemodynamic monitoring and careful monitoring of cardiac status are needed to avoid ischemia and other complications.

Chlorpheniramine; Hydrocodone; Phenylephrine: (Major) Avoid use of sympathomimetic agents with epoprostenol. Sympathomimetics counteract the medications used to stabilize pulmonary hypertension, including epoprostenol. Sympathomimetics can increase blood pressure, increase heart rate, and may cause vasoconstriction resulting in chest pain and shortness of breath in these patients. Patients should be advised to avoid amphetamine drugs, decongestants (including nasal decongestants) and sympathomimetic anorexiant for weight loss, including dietary supplements. Intravenous vasopressors may be used in the emergency management of pulmonary hypertension patients when needed, but hemodynamic monitoring and careful monitoring of cardiac status are needed to avoid ischemia and other complications.

Chlorpheniramine; Hydrocodone; Pseudoephedrine: (Major) Avoid use of sympathomimetic agents with epoprostenol. Sympathomimetics counteract the medications used to stabilize pulmonary hypertension, including epoprostenol. Sympathomimetics can increase blood pressure, increase heart rate, and may cause vasoconstriction resulting in chest pain and shortness of breath in these patients. Patients should be advised to avoid amphetamine drugs, decongestants (including nasal decongestants) and sympathomimetic anorexiant for weight loss, including dietary supplements. Intravenous vasopressors may be used in the emergency management of pulmonary hypertension patients when needed, but hemodynamic monitoring and careful monitoring of cardiac status are needed to avoid ischemia and other complications.

Chlorpheniramine; Ibuprofen; Pseudoephedrine: (Major) Avoid use of sympathomimetic agents with epoprostenol. Sympathomimetics counteract the medications used to stabilize pulmonary hypertension, including epoprostenol. Sympathomimetics can increase blood pressure, increase heart rate, and may cause vasoconstriction resulting in chest pain and shortness of breath in these patients. Patients should be advised to avoid amphetamine drugs, decongestants (including nasal decongestants) and sympathomimetic anorexiant for weight loss, including dietary supplements. Intravenous vasopressors may be used in the emergency management of pulmonary hypertension patients when needed, but hemodynamic monitoring and careful monitoring of cardiac status are needed to avoid ischemia and other complications. (Moderate) NSAIDs may decrease the effect of antihypertensive agents through various mechanisms, including renal and peripheral vasoactive pathways.

Chlorpheniramine; Phenylephrine: (Major) Avoid use of sympathomimetic agents with epoprostenol. Sympathomimetics counteract the medications used to stabilize pulmonary hypertension, including epoprostenol. Sympathomimetics can increase blood pressure, increase heart rate, and may cause vasoconstriction resulting in chest pain and shortness of breath in these patients. Patients should be advised to avoid amphetamine drugs, decongestants (including nasal decongestants) and sympathomimetic anorexiant for weight loss, including dietary supplements. Intravenous vasopressors may be used in the emergency management of pulmonary hypertension patients when needed, but hemodynamic monitoring and careful monitoring of cardiac status are needed to avoid ischemia and other complications.

Chlorpheniramine; Pseudoephedrine: (Major) Avoid use of sympathomimetic agents with epoprostenol. Sympathomimetics counteract the medications used to stabilize pulmonary hypertension, including epoprostenol. Sympathomimetics can increase blood pressure, increase heart rate, and may cause vasoconstriction resulting in chest pain and shortness of breath in these patients. Patients should be advised to avoid amphetamine drugs, decongestants (including nasal decongestants) and sympathomimetic anorexiant for weight loss, including dietary supplements. Intravenous vasopressors may be used in the emergency management of pulmonary hypertension patients when needed, but hemodynamic monitoring and careful monitoring of cardiac status are needed to avoid ischemia and other complications.

Chlorthalidone; Clonidine: (Moderate) The concomitant administration of epoprostenol with other antihypertensive agents can result in additive hypotensive effects. This can be therapeutically advantageous, but dosages must be adjusted accordingly.

Clevidipine: (Moderate) Calcium-channel blockers can have additive hypotensive effects with other antihypertensive agents. This additive effect can be desirable, but the patient should be monitored carefully and the dosage should be adjusted based on clinical response.

Clonidine: (Moderate) The concomitant administration of epoprostenol with other antihypertensive agents can result in additive hypotensive effects. This can be therapeutically advantageous, but dosages must be adjusted accordingly.

Clozapine: (Moderate) Clozapine used concomitantly with the antihypertensive agents can increase the risk and severity of hypotension by potentiating the effect of the antihypertensive drug.

Cocaine: (Major) Use of cocaine with antihypertensive agents may increase the antihypertensive effects of the antihypertensive medications or may potentiate cocaine-induced sympathetic stimulation.

Codeine; Guaifenesin; Pseudoephedrine: (Major) Avoid use of sympathomimetic agents with epoprostenol. Sympathomimetics counteract the medications used to stabilize pulmonary hypertension, including epoprostenol. Sympathomimetics can increase blood pressure, increase heart rate, and may cause vasoconstriction resulting in chest pain and shortness of breath in these patients. Patients should be advised to avoid amphetamine drugs, decongestants (including nasal decongestants) and sympathomimetic anorexiant for weight loss, including dietary supplements. Intravenous vasopressors may be used in the emergency management of pulmonary hypertension patients when needed, but hemodynamic monitoring and careful monitoring of cardiac status are needed to avoid ischemia and other complications.

Codeine; Phenylephrine; Promethazine: (Major) Avoid use of sympathomimetic agents with epoprostenol. Sympathomimetics counteract the medications used to stabilize pulmonary hypertension, including epoprostenol. Sympathomimetics can increase blood pressure, increase heart rate, and may cause vasoconstriction resulting in chest pain and shortness of breath in these patients. Patients should be advised to avoid amphetamine drugs, decongestants (including nasal decongestants) and sympathomimetic anorexiant for weight loss, including dietary supplements. Intravenous vasopressors may be used in the emergency management of pulmonary hypertension patients when needed, but hemodynamic monitoring and careful monitoring of cardiac status are needed to avoid ischemia and other complications.

Co-Enzyme Q10, Ubiquinone: (Moderate) Co-enzyme Q10, ubiquinone (CoQ10) may lower blood pressure. CoQ10 use in combination with antihypertensive agents may lead to additional reductions in blood pressure in some individuals. Patients who choose to take CoQ10 concurrently with antihypertensive medications should receive periodic blood pressure monitoring. Patients should be advised to inform their prescriber of their use of CoQ10.

Dabigatran: (Moderate) When used concurrently with anticoagulants, epoprostenol may increase the risk of bleeding.

Dalteparin: (Moderate) When used concurrently with anticoagulants, epoprostenol may increase the risk of bleeding.

Danaparoid: (Moderate) When used concurrently with anticoagulants, epoprostenol may increase the risk of bleeding.

Desirudin: (Moderate) When used concurrently with anticoagulants, epoprostenol may increase the risk of bleeding.

Desloratadine; Pseudoephedrine: (Major) Avoid use of sympathomimetic agents with epoprostenol. Sympathomimetics counteract the medications used to stabilize pulmonary hypertension, including epoprostenol. Sympathomimetics can increase blood pressure, increase heart rate, and may cause vasoconstriction resulting in chest pain and shortness of breath in these patients. Patients should be advised to avoid amphetamine drugs, decongestants (including nasal decongestants) and sympathomimetic anorexiant for weight loss, including dietary supplements. Intravenous vasopressors may be used in the emergency management of pulmonary hypertension patients when needed, but hemodynamic monitoring and careful monitoring of cardiac status are needed to avoid ischemia and other complications.

Dexbrompheniramine; Pseudoephedrine: (Major) Avoid use of sympathomimetic agents with epoprostenol. Sympathomimetics counteract the medications used to stabilize pulmonary hypertension, including epoprostenol. Sympathomimetics can increase blood pressure, increase heart rate, and may cause vasoconstriction resulting in chest pain and shortness of breath in these patients. Patients should be advised to avoid amphetamine drugs, decongestants (including nasal decongestants) and sympathomimetic anorexiant for weight loss, including dietary supplements. Intravenous vasopressors may be used in the emergency management of pulmonary hypertension patients when needed, but hemodynamic monitoring and careful monitoring of cardiac status are needed to avoid ischemia and other complications.

Dexchlorpheniramine; Dextromethorphan; Pseudoephedrine: (Major) Avoid use of sympathomimetic agents with epoprostenol. Sympathomimetics counteract the medications used to stabilize pulmonary hypertension, including epoprostenol. Sympathomimetics can increase blood pressure, increase heart rate, and may cause vasoconstriction resulting in chest pain and shortness of breath in these patients. Patients

should be advised to avoid amphetamine drugs, decongestants (including nasal decongestants) and sympathomimetic anorexiant for weight loss, including dietary supplements. Intravenous vasopressors may be used in the emergency management of pulmonary hypertension patients when needed, but hemodynamic monitoring and careful monitoring of cardiac status are needed to avoid ischemia and other complications.

Dexmethyphenidate: (Major) Avoid use of sympathomimetic agents with epoprostenol. Sympathomimetics counteract the medications used to stabilize pulmonary hypertension, including epoprostenol. Sympathomimetics can increase blood pressure, increase heart rate, and may cause vasoconstriction resulting in chest pain and shortness of breath in these patients. Patients should be advised to avoid amphetamine drugs, decongestants (including nasal decongestants) and sympathomimetic anorexiant for weight loss, including dietary supplements. Intravenous vasopressors may be used in the emergency management of pulmonary hypertension patients when needed, but hemodynamic monitoring and careful monitoring of cardiac status are needed to avoid ischemia and other complications.

Dextroamphetamine: (Major) Avoid use of sympathomimetic agents with epoprostenol. Sympathomimetics counteract the medications used to stabilize pulmonary hypertension, including epoprostenol. Sympathomimetics can increase blood pressure, increase heart rate, and may cause vasoconstriction resulting in chest pain and shortness of breath in these patients. Patients should be advised to avoid amphetamine drugs, decongestants (including nasal decongestants) and sympathomimetic anorexiant for weight loss, including dietary supplements. Intravenous vasopressors may be used in the emergency management of pulmonary hypertension patients when needed, but hemodynamic monitoring and careful monitoring of cardiac status are needed to avoid ischemia and other complications.

Dextromethorphan; Diphenhydramine; Phenylephrine: (Major) Avoid use of sympathomimetic agents with epoprostenol. Sympathomimetics counteract the medications used to stabilize pulmonary hypertension, including epoprostenol. Sympathomimetics can increase blood pressure, increase heart rate, and may cause vasoconstriction resulting in chest pain and shortness of breath in these patients. Patients should be advised to avoid amphetamine drugs, decongestants (including nasal decongestants) and sympathomimetic anorexiant for weight loss, including dietary supplements. Intravenous vasopressors may be used in the emergency management of pulmonary hypertension patients when needed, but hemodynamic monitoring and careful monitoring of cardiac status are needed to avoid ischemia and other complications.

Dextromethorphan; Guaifenesin; Phenylephrine: (Major) Avoid use of sympathomimetic agents with epoprostenol. Sympathomimetics counteract the medications used to stabilize pulmonary hypertension, including epoprostenol. Sympathomimetics can increase blood pressure, increase heart rate, and may cause vasoconstriction resulting in chest pain and shortness of breath in these patients. Patients should be advised to avoid amphetamine drugs, decongestants (including nasal decongestants) and sympathomimetic anorexiant for weight loss, including dietary supplements. Intravenous vasopressors may be used in the emergency management of pulmonary hypertension patients when needed, but hemodynamic monitoring and careful monitoring of cardiac status are needed to avoid ischemia and other complications.

Dextromethorphan; Guaifenesin; Pseudoephedrine: (Major) Avoid use of sympathomimetic agents with epoprostenol. Sympathomimetics counteract the medications used to stabilize pulmonary hypertension, including epoprostenol. Sympathomimetics can increase blood pressure, increase heart rate, and may cause vasoconstriction resulting in chest pain and shortness of breath in these patients. Patients should be advised to avoid amphetamine drugs, decongestants (including nasal decongestants) and sympathomimetic anorexiant for weight loss, including dietary supplements. Intravenous vasopressors may be used in the emergency management of pulmonary hypertension patients when needed, but hemodynamic monitoring and careful monitoring of cardiac status are needed to avoid ischemia and other complications.

Dextromethorphan; Quinidine: (Moderate) Quinidine can decrease blood pressure and should be used cautiously in patients receiving antihypertensive agents due to the potential for additive hypotension.

Diclofenac: (Moderate) NSAIDs may decrease the effect of antihypertensive agents through various mechanisms, including renal and peripheral vasoactive pathways.

Diclofenac; Misoprostol: (Moderate) NSAIDs may decrease the effect of antihypertensive agents through various mechanisms, including renal and peripheral vasoactive pathways.

Diethylpropion: (Major) Avoid use of sympathomimetic agents with epoprostenol. Sympathomimetics counteract the medications used to stabilize pulmonary hypertension, including epoprostenol. Sympathomimetics can increase blood pressure, increase heart rate, and may cause vasoconstriction resulting in chest pain and shortness of breath in these patients. Patients should be advised to avoid amphetamine drugs, decongestants (including nasal decongestants) and sympathomimetic anorexiant for weight loss, including dietary supplements. Intravenous vasopressors may be used in the emergency management of pulmonary hypertension patients when needed, but hemodynamic monitoring and careful monitoring of cardiac status are needed to avoid ischemia and other complications.

Diflunisal: (Moderate) NSAIDs may decrease the effect of antihypertensive agents through various mechanisms, including renal and peripheral vasoactive pathways.

Digoxin: (Moderate) Increased serum digoxin concentrations have been reported in patients who received digoxin and epoprostenol. Measure serum digoxin concentrations before initiating epoprostenol. Monitor patients who take both epoprostenol and digoxin for possible digoxin toxicity and reduce digoxin dose as necessary.

Dihydrocodeine; Guaifenesin; Pseudoephedrine: (Major) Avoid use of sympathomimetic agents with epoprostenol. Sympathomimetics counteract the medications used to stabilize pulmonary hypertension, including epoprostenol. Sympathomimetics can increase blood pressure, increase heart rate, and may cause vasoconstriction resulting in chest pain and shortness of breath in these patients. Patients should be advised to avoid amphetamine drugs, decongestants (including nasal decongestants) and sympathomimetic anorexiant for weight loss, including dietary supplements. Intravenous vasopressors may be used in the emergency management of pulmonary hypertension patients when needed, but hemodynamic monitoring and careful monitoring of cardiac status are needed to avoid ischemia and other complications.

Dihydroergotamine: (Minor) The combined use of vasodilators and the ergot alkaloids will likely result in antagonism of the vasoconstrictive effects of the ergot derivative. Clinically, for example, vasodilators may be used for supportive care of ergot alkaloid toxicity; with precautions to avoid hypotension.

Diltiazem: (Moderate) Calcium-channel blockers can have additive hypotensive effects with other antihypertensive agents. This additive effect can be desirable, but the patient should be monitored carefully and the dosage should be adjusted based on clinical response.

Diphenhydramine; Hydrocodone; Phenylephrine: (Major) Avoid use of sympathomimetic agents with epoprostenol. Sympathomimetics counteract the medications used to stabilize pulmonary hypertension, including epoprostenol. Sympathomimetics can increase blood pressure, increase heart rate, and may cause vasoconstriction resulting in chest pain and shortness of breath in these patients. Patients should be advised to avoid amphetamine drugs, decongestants (including nasal decongestants) and sympathomimetic anorexiant for weight loss, including dietary supplements. Intravenous vasopressors may be used in the emergency management of pulmonary hypertension patients when needed, but hemodynamic monitoring and careful monitoring of cardiac status are needed to avoid ischemia and other complications.

Diphenhydramine; Ibuprofen: (Moderate) NSAIDs may decrease the effect of antihypertensive agents through various mechanisms, including renal and peripheral vasoactive pathways.

Diphenhydramine; Naproxen: (Moderate) NSAIDs may decrease the effect of antihypertensive agents through various mechanisms, including renal and peripheral vasoactive pathways.

Diphenhydramine; Phenylephrine: (Major) Avoid use of sympathomimetic agents with epoprostenol. Sympathomimetics counteract the medications used to stabilize pulmonary hypertension, including epoprostenol. Sympathomimetics can increase blood pressure, increase heart rate, and may cause vasoconstriction resulting in chest pain and shortness of breath in these patients. Patients should be advised to avoid amphetamine drugs, decongestants (including nasal decongestants) and sympathomimetic anorexiant for weight loss, including dietary supplements. Intravenous vasopressors may be used in the emergency management of pulmonary hypertension patients when needed, but hemodynamic monitoring and careful monitoring of cardiac status are needed to avoid ischemia and other complications.

Dobutamine: (Major) Avoid use of sympathomimetic agents with epoprostenol. Sympathomimetics counteract the medications used to stabilize pulmonary hypertension, including epoprostenol. Sympathomimetics can increase blood pressure, increase heart rate, and may cause vasoconstriction resulting in chest pain and shortness of breath in these patients. Patients should be advised to avoid amphetamine drugs, decongestants (including nasal decongestants) and sympathomimetic anorexiant for weight loss, including dietary supplements. Intravenous vasopressors may be used in the emergency management of pulmonary hypertension patients when needed, but hemodynamic monitoring and careful monitoring of cardiac status are needed to avoid ischemia and other complications.

Dopamine: (Major) Avoid use of sympathomimetic agents with epoprostenol. Sympathomimetics counteract the medications used to stabilize pulmonary hypertension, including epoprostenol. Sympathomimetics can increase blood pressure, increase heart rate, and may cause vasoconstriction resulting in chest pain and shortness of breath in these patients. Patients should be advised to avoid amphetamine drugs, decongestants (including nasal decongestants) and sympathomimetic anorexiant for weight loss, including dietary supplements. Intravenous vasopressors may be used in the emergency management of pulmonary hypertension patients when needed, but hemodynamic monitoring and

careful monitoring of cardiac status are needed to avoid ischemia and other complications.

Dorzolamide; Timolol: (Moderate) Epoprostenol can have additive effects when administered with other antihypertensive agents, including beta-blockers. These effects can be used to therapeutic advantage, but dosage adjustments may be necessary.

Doxapram: (Major) Avoid use of sympathomimetic agents with epoprostenol. Sympathomimetics counteract the medications used to stabilize pulmonary hypertension, including epoprostenol. Sympathomimetics can increase blood pressure, increase heart rate, and may cause vasoconstriction resulting in chest pain and shortness of breath in these patients. Patients should be advised to avoid amphetamine drugs, decongestants (including nasal decongestants) and sympathomimetic anorexians for weight loss, including dietary supplements. Intravenous vasopressors may be used in the emergency management of pulmonary hypertension patients when needed, but hemodynamic monitoring and careful monitoring of cardiac status are needed to avoid ischemia and other complications.

Doxazosin: (Minor) Epoprostenol can have additive effects when administered with other antihypertensive agents, including alpha-blockers. These effects can be used to therapeutic advantage, but dosage adjustments may be necessary.

Duloxetine: (Moderate) Orthostatic hypotension and syncope have been reported during duloxetine administration. The concurrent administration of antihypertensive agents and duloxetine may increase the risk of hypotension. Monitor blood pressure if the combination is necessary.

Edoxaban: (Moderate) When used concurrently with anticoagulants, epoprostenol may increase the risk of bleeding.

Enalapril; Felodipine: (Moderate) Calcium-channel blockers can have additive hypotensive effects with other antihypertensive agents. This additive effect can be desirable, but the patient should be monitored carefully and the dosage should be adjusted based on clinical response.

Enflurane: (Moderate) General anesthetics can potentiate the hypotensive effects of antihypertensive agents.

Enoxaparin: (Moderate) When used concurrently with anticoagulants, epoprostenol may increase the risk of bleeding.

Ephedrine: (Major) Avoid use of sympathomimetic agents with epoprostenol. Sympathomimetics counteract the medications used to stabilize pulmonary hypertension, including epoprostenol. Sympathomimetics can increase blood pressure, increase heart rate, and may cause vasoconstriction resulting in chest pain and shortness of breath in these patients. Patients should be advised to avoid amphetamine drugs, decongestants (including nasal decongestants) and sympathomimetic anorexians for weight loss, including dietary supplements. Intravenous vasopressors may be used in the emergency management of pulmonary hypertension patients when needed, but hemodynamic monitoring and careful monitoring of cardiac status are needed to avoid ischemia and other complications.

Ephedrine; Guaifenesin: (Major) Avoid use of sympathomimetic agents with epoprostenol. Sympathomimetics counteract the medications used to stabilize pulmonary hypertension, including epoprostenol. Sympathomimetics can increase blood pressure, increase heart rate, and may cause vasoconstriction resulting in chest pain and shortness of breath in these patients. Patients should be advised to avoid amphetamine drugs, decongestants (including nasal decongestants) and sympathomimetic anorexians for weight loss, including dietary supplements. Intravenous vasopressors may be used in the emergency management of pulmonary hypertension patients when needed, but hemodynamic monitoring and careful monitoring of cardiac status are needed to avoid ischemia and other complications.

Epinephrine: (Major) Avoid use of sympathomimetic agents with epoprostenol. Sympathomimetics counteract the medications used to stabilize pulmonary hypertension, including epoprostenol. Sympathomimetics can increase blood pressure, increase heart rate, and may cause vasoconstriction resulting in chest pain and shortness of breath in these patients. Patients should be advised to avoid amphetamine drugs, decongestants (including nasal decongestants) and sympathomimetic anorexians for weight loss, including dietary supplements. Intravenous vasopressors may be used in the emergency management of pulmonary hypertension patients when needed, but hemodynamic monitoring and careful monitoring of cardiac status are needed to avoid ischemia and other complications.

Eplerenone: (Moderate) Epoprostenol can have additive effects when administered with other antihypertensive agents. These effects can be used to therapeutic advantage, but dosage adjustments may be necessary.

Eprosartan: (Moderate) Angiotensin II receptor antagonists can enhance the hypotensive effects of antihypertensive agents if given concomitantly. This additive effect may be desirable, but dosages must be adjusted accordingly.

Eprosartan; Hydrochlorothiazide, HCTZ: (Moderate) Angiotensin II receptor antagonists can enhance the hypotensive effects of antihypertensive agents if given concomitantly. This additive effect may be desirable, but dosages must be adjusted accordingly.

Esmolol: (Moderate) Epoprostenol can have additive effects when administered with other antihypertensive agents, including beta-blockers. These effects can be used to therapeutic advantage, but dosage adjustments may be necessary.

Etodolac: (Moderate) NSAIDs may decrease the effect of antihypertensive agents through various mechanisms, including renal and peripheral vasoactive pathways.

Etomidate: (Moderate) General anesthetics can potentiate the hypotensive effects of antihypertensive agents.

Famotidine; Ibuprofen: (Moderate) NSAIDs may decrease the effect of antihypertensive agents through various mechanisms, including renal and peripheral vasoactive pathways.

Felodipine: (Moderate) Calcium-channel blockers can have additive hypotensive effects with other antihypertensive agents. This additive effect can be desirable, but the patient should be monitored carefully and the dosage should be adjusted based on clinical response.

Fenoprofen: (Moderate) NSAIDs may decrease the effect of antihypertensive agents through various mechanisms, including renal and peripheral vasoactive pathways.

Flexofenadine; Pseudoephedrine: (Major) Avoid use of sympathomimetic agents with epoprostenol. Sympathomimetics counteract the medications used to stabilize pulmonary hypertension, including epoprostenol. Sympathomimetics can increase blood pressure, increase heart rate, and may cause vasoconstriction resulting in chest pain and shortness of breath in these patients. Patients should be advised to avoid amphetamine drugs, decongestants (including nasal decongestants) and sympathomimetic anorexians for weight loss, including dietary supplements. Intravenous vasopressors may be used in the emergency management of pulmonary hypertension patients when needed, but hemodynamic monitoring and careful monitoring of cardiac status are needed to avoid ischemia and other complications.

Fish Oil, Omega-3 Fatty Acids (Dietary Supplements): (Moderate) High doses of fish oil supplements may produce a blood pressure lowering effect. It is possible that additive reductions in blood pressure may be seen when fish oils are used in a patient already taking antihypertensive agents.

Flurbiprofen: (Moderate) NSAIDs may decrease the effect of antihypertensive agents through various mechanisms, including renal and peripheral vasoactive pathways.

Fondaparinux: (Moderate) When used concurrently with anticoagulants, epoprostenol may increase the risk of bleeding.

Fospropofol: (Moderate) General anesthetics can potentiate the hypotensive effects of antihypertensive agents.

Gallium Ga 68 Dotatate: (Moderate) Further reductions in blood pressure may occur when epoprostenol is administered with diuretics.

General anesthetics: (Moderate) General anesthetics can potentiate the hypotensive effects of antihypertensive agents.

Guaifenesin; Hydrocodone; Pseudoephedrine: (Major) Avoid use of sympathomimetic agents with epoprostenol. Sympathomimetics counteract the medications used to stabilize pulmonary hypertension, including epoprostenol. Sympathomimetics can increase blood pressure, increase heart rate, and may cause vasoconstriction resulting in chest pain and shortness of breath in these patients. Patients should be advised to avoid amphetamine drugs, decongestants (including nasal decongestants) and sympathomimetic anorexians for weight loss, including dietary supplements. Intravenous vasopressors may be used in the emergency management of pulmonary hypertension patients when needed, but hemodynamic monitoring and careful monitoring of cardiac status are needed to avoid ischemia and other complications.

Guaifenesin; Phenylephrine: (Major) Avoid use of sympathomimetic agents with epoprostenol. Sympathomimetics counteract the medications used to stabilize pulmonary hypertension, including epoprostenol. Sympathomimetics can increase blood pressure, increase heart rate, and may cause vasoconstriction resulting in chest pain and shortness of breath in these patients. Patients should be advised to avoid amphetamine drugs, decongestants (including nasal decongestants) and sympathomimetic anorexians for weight loss, including dietary supplements. Intravenous vasopressors may be used in the emergency management of pulmonary hypertension patients when needed, but hemodynamic monitoring and careful monitoring of cardiac status are needed to avoid ischemia and other complications.

Guaifenesin; Pseudoephedrine: (Major) Avoid use of sympathomimetic agents with epoprostenol. Sympathomimetics counteract the medications used to stabilize pulmonary hypertension, including epoprostenol. Sympathomimetics can increase blood pressure, increase heart rate, and may cause vasoconstriction resulting in chest pain and shortness of breath in these patients. Patients should be advised to avoid amphetamine drugs, decongestants (including nasal decongestants) and sympathomimetic anorexians for weight loss, including dietary supplements. Intravenous vasopressors may be used in the emergency management of pulmonary hypertension patients when needed, but hemodynamic monitoring and careful monitoring of cardiac status are needed to avoid ischemia and other complications.

Guanabenz: (Moderate) The concomitant administration of epoprostenol with other antihypertensive agents can result in additive hypotensive effects. This can be therapeutically advantageous, but dosages must be adjusted accordingly.

Guanfacine: (Moderate) The concomitant administration of epoprostenol with other antihypertensive agents can result in additive hypotensive effects. This can be therapeutically advantageous, but dosages must be adjusted accordingly.

Haloperidol: (Moderate) In general, haloperidol should be used cautiously with antihypertensive agents due to the possibility of additive hypotension.

Halothane: (Moderate) General anesthetics can potentiate the hypotensive effects of antihypertensive agents.

Heparin: (Moderate) When used concurrently with anticoagulants, epoprostenol may increase the risk of bleeding.

Hydralazine; Isosorbide Dinitrate, ISDN: (Moderate) Concomitant use of nitrates with other antihypertensive agents can cause additive hypotensive effects. Dosage adjustments may be necessary.

Hydrochlorothiazide, HCTZ; Methyldopa: (Moderate) The concomitant administration of epoprostenol with other antihypertensive agents can result in additive hypotensive effects. This can be therapeutically advantageous, but dosages must be adjusted accordingly.

Hydrocodone; Ibuprofen: (Moderate) NSAIDs may decrease the effect of antihypertensive agents through various mechanisms, including renal and peripheral vasoactive pathways.

Hydrocodone; Phenylephrine: (Major) Avoid use of sympathomimetic agents with epoprostenol. Sympathomimetics counteract the medications used to stabilize pulmonary hypertension, including epoprostenol. Sympathomimetics can increase blood pressure, increase heart rate, and may cause vasoconstriction resulting in chest pain and shortness of breath in these patients. Patients should be advised to avoid amphetamine drugs, decongestants (including nasal decongestants) and sympathomimetic anorexiant for weight loss, including dietary supplements. Intravenous vasopressors may be used in the emergency management of pulmonary hypertension patients when needed, but hemodynamic monitoring and careful monitoring of cardiac status are needed to avoid ischemia and other complications.

Hydrocodone; Potassium Guaiacolsulfonate; Pseudoephedrine: (Major) Avoid use of sympathomimetic agents with epoprostenol. Sympathomimetics counteract the medications used to stabilize pulmonary hypertension, including epoprostenol. Sympathomimetics can increase blood pressure, increase heart rate, and may cause vasoconstriction resulting in chest pain and shortness of breath in these patients. Patients should be advised to avoid amphetamine drugs, decongestants (including nasal decongestants) and sympathomimetic anorexiant for weight loss, including dietary supplements. Intravenous vasopressors may be used in the emergency management of pulmonary hypertension patients when needed, but hemodynamic monitoring and careful monitoring of cardiac status are needed to avoid ischemia and other complications.

Hydrocodone; Pseudoephedrine: (Major) Avoid use of sympathomimetic agents with epoprostenol. Sympathomimetics counteract the medications used to stabilize pulmonary hypertension, including epoprostenol. Sympathomimetics can increase blood pressure, increase heart rate, and may cause vasoconstriction resulting in chest pain and shortness of breath in these patients. Patients should be advised to avoid amphetamine drugs, decongestants (including nasal decongestants) and sympathomimetic anorexiant for weight loss, including dietary supplements. Intravenous vasopressors may be used in the emergency management of pulmonary hypertension patients when needed, but hemodynamic monitoring and careful monitoring of cardiac status are needed to avoid ischemia and other complications.

Ibuprofen: (Moderate) NSAIDs may decrease the effect of antihypertensive agents through various mechanisms, including renal and peripheral vasoactive pathways.

Ibuprofen; Oxycodone: (Moderate) NSAIDs may decrease the effect of antihypertensive agents through various mechanisms, including renal and peripheral vasoactive pathways.

Ibuprofen; Pseudoephedrine: (Major) Avoid use of sympathomimetic agents with epoprostenol. Sympathomimetics counteract the medications used to stabilize pulmonary hypertension, including epoprostenol. Sympathomimetics can increase blood pressure, increase heart rate, and may cause vasoconstriction resulting in chest pain and shortness of breath in these patients. Patients should be advised to avoid amphetamine drugs, decongestants (including nasal decongestants) and sympathomimetic anorexiant for weight loss, including dietary supplements. Intravenous vasopressors may be used in the emergency management of pulmonary hypertension patients when needed, but hemodynamic monitoring and careful monitoring of cardiac status are needed to avoid ischemia and other complications. (Moderate) NSAIDs may decrease the effect of antihypertensive agents through various mechanisms, including renal and peripheral vasoactive pathways.

Iloperidone: (Moderate) Secondary to alpha-blockade, iloperidone can produce vasodilation that may result in additive effects during concurrent use with antihypertensive agents. The potential reduction in blood pressure can precipitate orthostatic hypotension and associated dizziness, tachycardia, and syncope. If concurrent use of iloperidone and antihypertensive agents is necessary, patients should be counseled on measures to prevent orthostatic hypotension, such as sitting on the edge of the bed for several minutes prior to standing in the morning and rising slowly from a seated position. Close monitoring of blood pressure is recommended until the full effects of the combination therapy are known.

Iloprost: (Moderate) Epoprostenol can have additive effects when administered with other antihypertensive agents. These effects can be used to therapeutic advantage, but dosage adjustments may be necessary.

Indapamide: (Moderate) The effects of indapamide may be additive when administered with other antihypertensive agents or diuretics. This may be desirable, but occasionally orthostatic hypotension may occur. Dosages should be adjusted based on clinical response.

Indomethacin: (Moderate) NSAIDs may decrease the effect of antihypertensive agents through various mechanisms, including renal and peripheral vasoactive pathways.

Intravenous Lipid Emulsions: (Moderate) High doses of fish oil supplements may produce a blood pressure lowering effect. It is possible that additive reductions in blood pressure may be seen when fish oils are used in a patient already taking antihypertensive agents.

Irbesartan: (Moderate) Angiotensin II receptor antagonists can enhance the hypotensive effects of antihypertensive agents if given concomitantly. This additive effect may be desirable, but dosages must be adjusted accordingly.

Irbesartan; Hydrochlorothiazide, HCTZ: (Moderate) Angiotensin II receptor antagonists can enhance the hypotensive effects of antihypertensive agents if given concomitantly. This additive effect may be desirable, but dosages must be adjusted accordingly.

Isocarboxazid: (Moderate) Additive hypotensive effects may be seen when MAOIs are combined with antihypertensives or medications with hypotensive properties. Careful monitoring of blood pressure is suggested during concurrent therapy of MAOIs with epoprostenol.

Isoflurane: (Moderate) General anesthetics can potentiate the hypotensive effects of antihypertensive agents.

Isoproterenol: (Major) Avoid use of sympathomimetic agents with epoprostenol. Sympathomimetics counteract the medications used to stabilize pulmonary hypertension, including epoprostenol. Sympathomimetics can increase blood pressure, increase heart rate, and may cause vasoconstriction resulting in chest pain and shortness of breath in these patients. Patients should be advised to avoid amphetamine drugs, decongestants (including nasal decongestants) and sympathomimetic anorexiant for weight loss, including dietary supplements. Intravenous vasopressors may be used in the emergency management of pulmonary hypertension patients when needed, but hemodynamic monitoring and careful monitoring of cardiac status are needed to avoid ischemia and other complications.

Isosorbide Dinitrate, ISDN: (Moderate) Concomitant use of nitrates with other antihypertensive agents can cause additive hypotensive effects. Dosage adjustments may be necessary.

Isosorbide Mononitrate: (Moderate) Concomitant use of nitrates with other antihypertensive agents can cause additive hypotensive effects. Dosage adjustments may be necessary.

Isradipine: (Moderate) Calcium-channel blockers can have additive hypotensive effects with other antihypertensive agents. This additive effect can be desirable, but the patient should be monitored carefully and the dosage should be adjusted based on clinical response.

Ketamine: (Moderate) General anesthetics can potentiate the hypotensive effects of antihypertensive agents.

Ketoprofen: (Moderate) NSAIDs may decrease the effect of antihypertensive agents through various mechanisms, including renal and peripheral vasoactive pathways.

Ketorolac: (Moderate) NSAIDs may decrease the effect of antihypertensive agents through various mechanisms, including renal and peripheral vasoactive pathways.

Labetalol: (Moderate) Epoprostenol can have additive effects when administered with other antihypertensive agents, including beta-blockers. These effects can be used to therapeutic advantage, but dosage adjustments may be necessary.

Lansoprazole; Naproxen: (Moderate) NSAIDs may decrease the effect of antihypertensive agents through various mechanisms, including renal and peripheral vasoactive pathways.

Lepirudin: (Moderate) When used concurrently with anticoagulants, epoprostenol may increase the risk of bleeding.

Levamlodipine: (Moderate) Calcium-channel blockers can have additive hypotensive effects with other antihypertensive agents. This additive effect can be desirable, but the patient should be monitored carefully and the dosage should be adjusted based on clinical response.

Levobetaxolol: (Moderate) Epoprostenol can have additive effects when administered with other antihypertensive agents, including beta-blockers. These effects can be used to therapeutic advantage, but dosage adjustments may be necessary.

Levobunolol: (Moderate) Epoprostenol can have additive effects when administered with other antihypertensive agents, including beta-blockers.

These effects can be used to therapeutic advantage, but dosage adjustments may be necessary.

Levodopa: (Moderate) Concomitant use of antihypertensive agents with levodopa can result in additive hypotensive effects.

Lisdexamfetamine: (Major) Avoid use of sympathomimetic agents with epoprostenol. Sympathomimetics counteract the medications used to stabilize pulmonary hypertension, including epoprostenol. Sympathomimetics can increase blood pressure, increase heart rate, and may cause vasoconstriction resulting in chest pain and shortness of breath in these patients. Patients should be advised to avoid amphetamine drugs, decongestants (including nasal decongestants) and sympathomimetic anorexiant for weight loss, including dietary supplements. Intravenous vasopressors may be used in the emergency management of pulmonary hypertension patients when needed, but hemodynamic monitoring and careful monitoring of cardiac status are needed to avoid ischemia and other complications.

Loop diuretics: (Moderate) Epoprostenol can have additive effects when administered with other antihypertensive agents. These effects can be used to therapeutic advantage, but dosage adjustments may be necessary.

Loratadine; Pseudoephedrine: (Major) Avoid use of sympathomimetic agents with epoprostenol. Sympathomimetics counteract the medications used to stabilize pulmonary hypertension, including epoprostenol. Sympathomimetics can increase blood pressure, increase heart rate, and may cause vasoconstriction resulting in chest pain and shortness of breath in these patients. Patients should be advised to avoid amphetamine drugs, decongestants (including nasal decongestants) and sympathomimetic anorexiant for weight loss, including dietary supplements. Intravenous vasopressors may be used in the emergency management of pulmonary hypertension patients when needed, but hemodynamic monitoring and careful monitoring of cardiac status are needed to avoid ischemia and other complications.

Losartan: (Moderate) Angiotensin II receptor antagonists can enhance the hypotensive effects of antihypertensive agents if given concomitantly. This additive effect may be desirable, but dosages must be adjusted accordingly.

Losartan; Hydrochlorothiazide, HCTZ: (Moderate) Angiotensin II receptor antagonists can enhance the hypotensive effects of antihypertensive agents if given concomitantly. This additive effect may be desirable, but dosages must be adjusted accordingly.

Lovastatin; Niacin: (Moderate) Cutaneous vasodilation induced by niacin may become problematic if high-dose niacin is used concomitantly with other antihypertensive agents, especially epoprostenol. This effect is of particular concern in the setting of acute myocardial infarction, unstable angina, or other acute hemodynamic compromise.

Lurasidone: (Moderate) Due to the antagonism of lurasidone at alpha-1 adrenergic receptors, the drug may enhance the hypotensive effects of alpha-blockers and other antihypertensive agents. If concurrent use of lurasidone and antihypertensive agents is necessary, patients should be counseled on measures to prevent orthostatic hypotension, such as sitting on the edge of the bed for several minutes prior to standing in the morning and rising slowly from a seated position. Close monitoring of blood pressure is recommended until the full effects of the combination therapy are known.

Mannitol: (Moderate) Further reductions in blood pressure may occur when epoprostenol is administered with diuretics.

Mecamylamine: (Moderate) Epoprostenol can have additive effects when administered with other antihypertensive agents. These effects can be used to therapeutic advantage, but dosage adjustments may be necessary.

Meclofenamate Sodium: (Moderate) NSAIDs may decrease the effect of antihypertensive agents through various mechanisms, including renal and peripheral vasoactive pathways.

Mefenamic Acid: (Moderate) NSAIDs may decrease the effect of antihypertensive agents through various mechanisms, including renal and peripheral vasoactive pathways.

Meloxicam: (Moderate) NSAIDs may decrease the effect of antihypertensive agents through various mechanisms, including renal and peripheral vasoactive pathways.

Mepivacaine; Levonordefrin: (Major) Avoid use of sympathomimetic agents with epoprostenol. Sympathomimetics counteract the medications used to stabilize pulmonary hypertension, including epoprostenol. Sympathomimetics can increase blood pressure, increase heart rate, and may cause vasoconstriction resulting in chest pain and shortness of breath in these patients. Patients should be advised to avoid amphetamine drugs, decongestants (including nasal decongestants) and sympathomimetic anorexiant for weight loss, including dietary supplements. Intravenous vasopressors may be used in the emergency management of pulmonary hypertension patients when needed, but hemodynamic monitoring and careful monitoring of cardiac status are needed to avoid ischemia and other complications.

Methamphetamine: (Major) Avoid use of sympathomimetic agents with epoprostenol. Sympathomimetics counteract the medications used to stabilize pulmonary hypertension, including epoprostenol. Sympathomimetics can increase blood pressure, increase heart rate, and may cause vasoconstriction resulting in chest pain and shortness of breath in these patients. Patients should be advised to avoid amphetamine drugs, decongestants (including nasal decongestants) and sympathomimetic anorexiant for weight loss, including dietary supplements. Intravenous vasopressors may be used in the emergency management of pulmonary hypertension patients when needed, but hemodynamic monitoring and careful monitoring of cardiac status are needed to avoid ischemia and other complications.

Methazolamide: (Moderate) Further reductions in blood pressure may occur when epoprostenol is administered with other antihypertensive agents.

Methohexital: (Moderate) Concurrent use of methohexital and antihypertensive agents increases the risk of developing hypotension.

Methyldopa: (Moderate) The concomitant administration of epoprostenol with other antihypertensive agents can result in additive hypotensive effects. This can be therapeutically advantageous, but dosages must be adjusted accordingly.

Methylphenidate: (Major) Avoid use of sympathomimetic agents with epoprostenol. Sympathomimetics counteract the medications used to stabilize pulmonary hypertension, including epoprostenol. Sympathomimetics can increase blood pressure, increase heart rate, and may cause vasoconstriction resulting in chest pain and shortness of breath in these patients. Patients should be advised to avoid amphetamine drugs, decongestants (including nasal decongestants) and sympathomimetic anorexiant for weight loss, including dietary supplements. Intravenous vasopressors may be used in the emergency management of pulmonary hypertension patients when needed, but hemodynamic monitoring and careful monitoring of cardiac status are needed to avoid ischemia and other complications.

Metoprolol: (Moderate) Epoprostenol can have additive effects when administered with other antihypertensive agents, including beta-blockers. These effects can be used to therapeutic advantage, but dosage adjustments may be necessary.

Metoprolol; Hydrochlorothiazide, HCTZ: (Moderate) Epoprostenol can have additive effects when administered with other antihypertensive agents, including beta-blockers. These effects can be used to therapeutic advantage, but dosage adjustments may be necessary.

Midodrine: (Major) Avoid use of sympathomimetic agents with epoprostenol. Sympathomimetics counteract the medications used to stabilize pulmonary hypertension, including epoprostenol. Sympathomimetics can increase blood pressure, increase heart rate, and may cause vasoconstriction resulting in chest pain and shortness of breath in these patients. Patients should be advised to avoid amphetamine drugs, decongestants (including nasal decongestants) and sympathomimetic anorexiant for weight loss, including dietary supplements. Intravenous vasopressors may be used in the emergency management of pulmonary hypertension patients when needed, but hemodynamic monitoring and careful monitoring of cardiac status are needed to avoid ischemia and other complications.

Milrinone: (Moderate) Concurrent administration of antihypertensive agents could lead to additive hypotension when administered with milrinone. Titrate milrinone dosage according to hemodynamic response.

Monoamine oxidase inhibitors: (Moderate) Additive hypotensive effects may be seen when MAOIs are combined with antihypertensives or medications with hypotensive properties. Careful monitoring of blood pressure is suggested during concurrent therapy of MAOIs with epoprostenol.

Nabumetone: (Moderate) NSAIDs may decrease the effect of antihypertensive agents through various mechanisms, including renal and peripheral vasoactive pathways.

Nadolol: (Moderate) Epoprostenol can have additive effects when administered with other antihypertensive agents, including beta-blockers. These effects can be used to therapeutic advantage, but dosage adjustments may be necessary.

Naproxen: (Moderate) NSAIDs may decrease the effect of antihypertensive agents through various mechanisms, including renal and peripheral vasoactive pathways.

Naproxen; Esomeprazole: (Moderate) NSAIDs may decrease the effect of antihypertensive agents through various mechanisms, including renal and peripheral vasoactive pathways.

Naproxen; Pseudoephedrine: (Major) Avoid use of sympathomimetic agents with epoprostenol. Sympathomimetics counteract the medications used to stabilize pulmonary hypertension, including epoprostenol. Sympathomimetics can increase blood pressure, increase heart rate, and may cause vasoconstriction resulting in chest pain and shortness of breath in these patients. Patients should be advised to avoid amphetamine drugs, decongestants (including nasal decongestants) and sympathomimetic anorexiant for weight loss, including dietary supplements. Intravenous vasopressors may be used in the emergency management of pulmonary hypertension patients when needed, but hemodynamic monitoring and careful monitoring of cardiac status are needed to avoid ischemia and other complications. (Moderate) NSAIDs may decrease the effect of

antihypertensive agents through various mechanisms, including renal and peripheral vasoactive pathways.

Nebivolol: (Moderate) Epoprostenol can have additive effects when administered with other antihypertensive agents, including beta-blockers. These effects can be used to therapeutic advantage, but dosage adjustments may be necessary.

Nebivolol; Valsartan: (Moderate) Angiotensin II receptor antagonists can enhance the hypotensive effects of antihypertensive agents if given concomitantly. This additive effect may be desirable, but dosages must be adjusted accordingly. (Moderate) Epoprostenol can have additive effects when administered with other antihypertensive agents, including beta-blockers. These effects can be used to therapeutic advantage, but dosage adjustments may be necessary.

Nesiritide, BNP: (Major) The potential for hypotension may be increased when coadministering nesiritide with antihypertensive agents.

Niacin, Niacinamide: (Moderate) Cutaneous vasodilation induced by niacin may become problematic if high-dose niacin is used concomitantly with other antihypertensive agents, especially epoprostenol. This effect is of particular concern in the setting of acute myocardial infarction, unstable angina, or other acute hemodynamic compromise.

Niacin; Simvastatin: (Moderate) Cutaneous vasodilation induced by niacin may become problematic if high-dose niacin is used concomitantly with other antihypertensive agents, especially epoprostenol. This effect is of particular concern in the setting of acute myocardial infarction, unstable angina, or other acute hemodynamic compromise.

Nicardipine: (Moderate) Calcium-channel blockers can have additive hypotensive effects with other antihypertensive agents. This additive effect can be desirable, but the patient should be monitored carefully and the dosage should be adjusted based on clinical response.

Nifedipine: (Moderate) Calcium-channel blockers can have additive hypotensive effects with other antihypertensive agents. This additive effect can be desirable, but the patient should be monitored carefully and the dosage should be adjusted based on clinical response.

Nimodipine: (Moderate) Calcium-channel blockers can have additive hypotensive effects with other antihypertensive agents. This additive effect can be desirable, but the patient should be monitored carefully and the dosage should be adjusted based on clinical response.

Nisoldipine: (Moderate) Calcium-channel blockers can have additive hypotensive effects with other antihypertensive agents. This additive effect can be desirable, but the patient should be monitored carefully and the dosage should be adjusted based on clinical response.

Nitrates: (Moderate) Concomitant use of nitrates with other antihypertensive agents can cause additive hypotensive effects. Dosage adjustments may be necessary.

Nitroglycerin: (Moderate) Concomitant use of nitrates with other antihypertensive agents can cause additive hypotensive effects. Dosage adjustments may be necessary.

Nonsteroidal antiinflammatory drugs: (Moderate) NSAIDs may decrease the effect of antihypertensive agents through various mechanisms, including renal and peripheral vasoactive pathways.

Norepinephrine: (Major) Avoid use of sympathomimetic agents with epoprostenol. Sympathomimetics counteract the medications used to stabilize pulmonary hypertension, including epoprostenol. Sympathomimetics can increase blood pressure, increase heart rate, and may cause vasoconstriction resulting in chest pain and shortness of breath in these patients. Patients should be advised to avoid amphetamine drugs, decongestants (including nasal decongestants) and sympathomimetic anorexiant for weight loss, including dietary supplements. Intravenous vasopressors may be used in the emergency management of pulmonary hypertension patients when needed, but hemodynamic monitoring and careful monitoring of cardiac status are needed to avoid ischemia and other complications.

Olanzapine: (Moderate) Olanzapine may induce orthostatic hypotension and thus enhance the effects of antihypertensive agents.

Olanzapine; Fluoxetine: (Moderate) Olanzapine may induce orthostatic hypotension and thus enhance the effects of antihypertensive agents.

Olanzapine; Samidorphan: (Moderate) Olanzapine may induce orthostatic hypotension and thus enhance the effects of antihypertensive agents.

Olmesartan: (Moderate) Angiotensin II receptor antagonists can enhance the hypotensive effects of antihypertensive agents if given concomitantly. This additive effect may be desirable, but dosages must be adjusted accordingly.

Olmesartan; Amlodipine; Hydrochlorothiazide, HCTZ: (Moderate) Angiotensin II receptor antagonists can enhance the hypotensive effects of antihypertensive agents if given concomitantly. This additive effect may be desirable, but dosages must be adjusted accordingly. (Moderate) Calcium-channel blockers can have additive hypotensive effects with other antihypertensive agents. This additive effect can be desirable, but the patient should be monitored carefully and the dosage should be adjusted based on clinical response.

Olmesartan; Hydrochlorothiazide, HCTZ: (Moderate) Angiotensin II receptor antagonists can enhance the hypotensive effects of antihypertensive agents if given concomitantly. This additive effect may be desirable, but dosages must be adjusted accordingly.

Oxaprozin: (Moderate) NSAIDs may decrease the effect of antihypertensive agents through various mechanisms, including renal and peripheral vasoactive pathways.

Oxymetazoline: (Major) The vasoconstricting actions of oxymetazoline, an alpha adrenergic agonist, may reduce the antihypertensive effects produced by epoprostenol. If these drugs are used together, closely monitor for changes in blood pressure.

Pemoline: (Major) Avoid use of sympathomimetic agents with epoprostenol. Sympathomimetics counteract the medications used to stabilize pulmonary hypertension, including epoprostenol. Sympathomimetics can increase blood pressure, increase heart rate, and may cause vasoconstriction resulting in chest pain and shortness of breath in these patients. Patients should be advised to avoid amphetamine drugs, decongestants (including nasal decongestants) and sympathomimetic anorexiant for weight loss, including dietary supplements. Intravenous vasopressors may be used in the emergency management of pulmonary hypertension patients when needed, but hemodynamic monitoring and careful monitoring of cardiac status are needed to avoid ischemia and other complications.

Penbutolol: (Moderate) Epoprostenol can have additive effects when administered with other antihypertensive agents, including beta-blockers. These effects can be used to therapeutic advantage, but dosage adjustments may be necessary.

Pentosan: (Moderate) When used concurrently with anticoagulants, epoprostenol may increase the risk of bleeding.

Pentoxifylline: (Moderate) Pentoxifylline has been used concurrently with antihypertensive drugs (beta blockers, diuretics) without observed problems. Small decreases in blood pressure have been observed in some patients treated with pentoxifylline; periodic systemic blood pressure monitoring is recommended for patients receiving concomitant antihypertensives. If indicated, dosage of the antihypertensive agents should be reduced.

Perindopril; Amlodipine: (Moderate) Calcium-channel blockers can have additive hypotensive effects with other antihypertensive agents. This additive effect can be desirable, but the patient should be monitored carefully and the dosage should be adjusted based on clinical response.

Phendimetrazine: (Major) Avoid use of sympathomimetic agents with epoprostenol. Sympathomimetics counteract the medications used to stabilize pulmonary hypertension, including epoprostenol. Sympathomimetics can increase blood pressure, increase heart rate, and may cause vasoconstriction resulting in chest pain and shortness of breath in these patients. Patients should be advised to avoid amphetamine drugs, decongestants (including nasal decongestants) and sympathomimetic anorexiant for weight loss, including dietary supplements. Intravenous vasopressors may be used in the emergency management of pulmonary hypertension patients when needed, but hemodynamic monitoring and careful monitoring of cardiac status are needed to avoid ischemia and other complications.

Phenelzine: (Moderate) Additive hypotensive effects may be seen when MAOIs are combined with antihypertensives or medications with hypotensive properties. Careful monitoring of blood pressure is suggested during concurrent therapy of MAOIs with epoprostenol.

Phenoxybenzamine: (Minor) Epoprostenol can have additive effects when administered with other antihypertensive agents, including alpha-blockers. These effects can be used to therapeutic advantage, but dosage adjustments may be necessary.

Phentermine: (Major) Avoid use of sympathomimetic agents with epoprostenol. Sympathomimetics counteract the medications used to stabilize pulmonary hypertension, including epoprostenol. Sympathomimetics can increase blood pressure, increase heart rate, and may cause vasoconstriction resulting in chest pain and shortness of breath in these patients. Patients should be advised to avoid amphetamine drugs, decongestants (including nasal decongestants) and sympathomimetic anorexiant for weight loss, including dietary supplements. Intravenous vasopressors may be used in the emergency management of pulmonary hypertension patients when needed, but hemodynamic monitoring and careful monitoring of cardiac status are needed to avoid ischemia and other complications.

Phentermine; Topiramate: (Major) Avoid use of sympathomimetic agents with epoprostenol. Sympathomimetics counteract the medications used to stabilize pulmonary hypertension, including epoprostenol. Sympathomimetics can increase blood pressure, increase heart rate, and may cause vasoconstriction resulting in chest pain and shortness of breath in these patients. Patients should be advised to avoid amphetamine drugs, decongestants (including nasal decongestants) and sympathomimetic anorexiant for weight loss, including dietary supplements. Intravenous vasopressors may be used in the emergency management of pulmonary hypertension patients when needed, but hemodynamic monitoring and careful monitoring of cardiac status are needed to avoid ischemia and other complications.

Phentolamine: (Minor) Epoprostenol can have additive effects when administered with other antihypertensive agents, including alpha-blockers. These effects can be used to therapeutic advantage, but dosage adjustments may be necessary.

Phenylephrine: (Major) Avoid use of sympathomimetic agents with epoprostenol. Sympathomimetics counteract the medications used to stabilize pulmonary hypertension, including epoprostenol. Sympathomimetics can increase blood pressure, increase heart rate, and may cause vasoconstriction resulting in chest pain and shortness of breath in these patients. Patients should be advised to avoid amphetamine drugs, decongestants (including nasal decongestants) and sympathomimetic anorexiant for weight loss, including dietary supplements. Intravenous vasopressors may be used in the emergency management of pulmonary hypertension patients when needed, but hemodynamic monitoring and careful monitoring of cardiac status are needed to avoid ischemia and other complications.

Pindolol: (Moderate) Epoprostenol can have additive effects when administered with other antihypertensive agents, including beta-blockers. These effects can be used to therapeutic advantage, but dosage adjustments may be necessary.

Piroxicam: (Moderate) NSAIDs may decrease the effect of antihypertensive agents through various mechanisms, including renal and peripheral vasoactive pathways.

Potassium-sparing diuretics: (Moderate) Epoprostenol can have additive effects when administered with other antihypertensive agents. These effects can be used to therapeutic advantage, but dosage adjustments may be necessary.

Prazosin: (Minor) Epoprostenol can have additive effects when administered with other antihypertensive agents, including alpha-blockers. These effects can be used to therapeutic advantage, but dosage adjustments may be necessary.

Prilocaine; Epinephrine: (Major) Avoid use of sympathomimetic agents with epoprostenol. Sympathomimetics counteract the medications used to stabilize pulmonary hypertension, including epoprostenol. Sympathomimetics can increase blood pressure, increase heart rate, and may cause vasoconstriction resulting in chest pain and shortness of breath in these patients. Patients should be advised to avoid amphetamine drugs, decongestants (including nasal decongestants) and sympathomimetic anorexiant for weight loss, including dietary supplements. Intravenous vasopressors may be used in the emergency management of pulmonary hypertension patients when needed, but hemodynamic monitoring and careful monitoring of cardiac status are needed to avoid ischemia and other complications.

Procainamide: (Moderate) Procainamide can decrease blood pressure and should be used cautiously in patients receiving antihypertensive agents. Intravenous administration of procainamide is more likely to cause hypotensive effects.

Procaine: (Moderate) Local anesthetics may cause additive hypotension in combination with antihypertensive agents.

Promethazine; Phenylephrine: (Major) Avoid use of sympathomimetic agents with epoprostenol. Sympathomimetics counteract the medications used to stabilize pulmonary hypertension, including epoprostenol. Sympathomimetics can increase blood pressure, increase heart rate, and may cause vasoconstriction resulting in chest pain and shortness of breath in these patients. Patients should be advised to avoid amphetamine drugs, decongestants (including nasal decongestants) and sympathomimetic anorexiant for weight loss, including dietary supplements. Intravenous vasopressors may be used in the emergency management of pulmonary hypertension patients when needed, but hemodynamic monitoring and careful monitoring of cardiac status are needed to avoid ischemia and other complications.

Propofol: (Moderate) General anesthetics can potentiate the hypotensive effects of antihypertensive agents.

Propranolol: (Moderate) Epoprostenol can have additive effects when administered with other antihypertensive agents, including beta-blockers. These effects can be used to therapeutic advantage, but dosage adjustments may be necessary.

Propranolol; Hydrochlorothiazide, HCTZ: (Moderate) Epoprostenol can have additive effects when administered with other antihypertensive agents, including beta-blockers. These effects can be used to therapeutic advantage, but dosage adjustments may be necessary.

Pseudoephedrine: (Major) Avoid use of sympathomimetic agents with epoprostenol. Sympathomimetics counteract the medications used to stabilize pulmonary hypertension, including epoprostenol. Sympathomimetics can increase blood pressure, increase heart rate, and may cause vasoconstriction resulting in chest pain and shortness of breath in these patients. Patients should be advised to avoid amphetamine drugs, decongestants (including nasal decongestants) and sympathomimetic anorexiant for weight loss, including dietary supplements. Intravenous vasopressors may be used in the emergency management of pulmonary hypertension patients when needed, but hemodynamic monitoring and careful monitoring of cardiac status are needed to avoid ischemia and other complications.

Pseudoephedrine; Triprolidine: (Major) Avoid use of sympathomimetic agents with epoprostenol. Sympathomimetics counteract the medications used to stabilize pulmonary hypertension, including epoprostenol. Sympathomimetics can increase blood pressure, increase heart rate, and may cause vasoconstriction resulting in chest pain and shortness of breath in these patients. Patients should be advised to avoid amphetamine drugs, decongestants (including nasal decongestants) and sympathomimetic anorexiant for weight loss, including dietary supplements. Intravenous vasopressors may be used in the emergency management of pulmonary hypertension patients when needed, but hemodynamic monitoring and careful monitoring of cardiac status are needed to avoid ischemia and other complications.

Quinidine: (Moderate) Quinidine can decrease blood pressure and should be used cautiously in patients receiving antihypertensive agents due to the potential for additive hypotension.

Racepinephrine: (Major) Avoid use of sympathomimetic agents with epoprostenol. Sympathomimetics counteract the medications used to stabilize pulmonary hypertension, including epoprostenol. Sympathomimetics can increase blood pressure, increase heart rate, and may cause vasoconstriction resulting in chest pain and shortness of breath in these patients. Patients should be advised to avoid amphetamine drugs, decongestants (including nasal decongestants) and sympathomimetic anorexiant for weight loss, including dietary supplements. Intravenous vasopressors may be used in the emergency management of pulmonary hypertension patients when needed, but hemodynamic monitoring and careful monitoring of cardiac status are needed to avoid ischemia and other complications.

Rasagiline: (Moderate) Additive hypotensive effects may be seen when monoamine oxidase inhibitors (MAOIs) are combined with antihypertensives or medications with hypotensive properties. Careful monitoring of blood pressure is suggested during concurrent therapy of MAOIs with vasodilators. Patients should be instructed to rise slowly from a sitting position, and to report syncope or changes in blood pressure or heart rate to their health care provider.

Reserpine: (Moderate) Epoprostenol can have additive effects when administered with other antihypertensive agents. These effects can be used to therapeutic advantage, but dosage adjustments may be necessary.

Risperidone: (Moderate) Risperidone may induce orthostatic hypotension and thus enhance the hypotensive effects of antihypertensive agents. Lower initial doses or slower dose titration of risperidone may be necessary in patients receiving antihypertensive agents concomitantly.

Ritodrine: (Major) Avoid use of sympathomimetic agents with epoprostenol. Sympathomimetics counteract the medications used to stabilize pulmonary hypertension, including epoprostenol. Sympathomimetics can increase blood pressure, increase heart rate, and may cause vasoconstriction resulting in chest pain and shortness of breath in these patients. Patients should be advised to avoid amphetamine drugs, decongestants (including nasal decongestants) and sympathomimetic anorexiant for weight loss, including dietary supplements. Intravenous vasopressors may be used in the emergency management of pulmonary hypertension patients when needed, but hemodynamic monitoring and careful monitoring of cardiac status are needed to avoid ischemia and other complications.

Rivaroxaban: (Moderate) When used concurrently with anticoagulants, epoprostenol may increase the risk of bleeding.

Rofecoxib: (Moderate) NSAIDs may decrease the effect of antihypertensive agents through various mechanisms, including renal and peripheral vasoactive pathways.

Sacubitril; Valsartan: (Moderate) Angiotensin II receptor antagonists can enhance the hypotensive effects of antihypertensive agents if given concomitantly. This additive effect may be desirable, but dosages must be adjusted accordingly.

Serdexmethylphenidate; Dexmethylphenidate: (Major) Avoid use of sympathomimetic agents with epoprostenol. Sympathomimetics counteract the medications used to stabilize pulmonary hypertension, including epoprostenol. Sympathomimetics can increase blood pressure, increase heart rate, and may cause vasoconstriction resulting in chest pain and shortness of breath in these patients. Patients should be advised to avoid amphetamine drugs, decongestants (including nasal decongestants) and sympathomimetic anorexiant for weight loss, including dietary supplements. Intravenous vasopressors may be used in the emergency management of pulmonary hypertension patients when needed, but hemodynamic monitoring and careful monitoring of cardiac status are needed to avoid ischemia and other complications.

Sevoflurane: (Moderate) General anesthetics can potentiate the hypotensive effects of antihypertensive agents.

Silodosin: (Moderate) During clinical trials with silodosin, the incidence of dizziness and orthostatic hypotension was higher in patients receiving concomitant antihypertensive treatment. Thus, caution is advisable when silodosin is administered with antihypertensive agents.

Sotalol: (Moderate) Epoprostenol can have additive effects when administered with other antihypertensive agents, including beta-blockers. These effects can be used to therapeutic advantage, but dosage adjustments may be necessary.

Sulindac: (Moderate) NSAIDs may decrease the effect of antihypertensive agents through various mechanisms, including renal and peripheral vasoactive pathways.

Sumatriptan; Naproxen: (Moderate) NSAIDs may decrease the effect of antihypertensive agents through various mechanisms, including renal and peripheral vasoactive pathways.

Sympathomimetics: (Major) Avoid use of sympathomimetic agents with epoprostenol. Sympathomimetics counteract the medications used to stabilize pulmonary hypertension, including epoprostenol. Sympathomimetics can increase blood pressure, increase heart rate, and may cause vasoconstriction resulting in chest pain and shortness of breath in these patients. Patients should be advised to avoid amphetamine drugs, decongestants (including nasal decongestants) and sympathomimetic anorexigants for weight loss, including dietary supplements. Intravenous vasopressors may be used in the emergency management of pulmonary hypertension patients when needed, but hemodynamic monitoring and careful monitoring of cardiac status are needed to avoid ischemia and other complications.

Telmisartan: (Moderate) Angiotensin II receptor antagonists can enhance the hypotensive effects of antihypertensive agents if given concomitantly. This additive effect may be desirable, but dosages must be adjusted accordingly.

Telmisartan; Amlodipine: (Moderate) Angiotensin II receptor antagonists can enhance the hypotensive effects of antihypertensive agents if given concomitantly. This additive effect may be desirable, but dosages must be adjusted accordingly. (Moderate) Calcium-channel blockers can have additive hypotensive effects with other antihypertensive agents. This additive effect can be desirable, but the patient should be monitored carefully and the dosage should be adjusted based on clinical response.

Telmisartan; Hydrochlorothiazide, HCTZ: (Moderate) Angiotensin II receptor antagonists can enhance the hypotensive effects of antihypertensive agents if given concomitantly. This additive effect may be desirable, but dosages must be adjusted accordingly.

Terazosin: (Minor) Epoprostenol can have additive effects when administered with other antihypertensive agents, including alpha-blockers. These effects can be used to therapeutic advantage, but dosage adjustments may be necessary.

Tetracaine: (Moderate) Local anesthetics may cause additive hypotension in combination with antihypertensive agents. Use extreme caution with the concomitant use of tetracaine and antihypertensive agents.

Thiopental: (Moderate) Concurrent use of thiopental and alpha-blockers or antihypertensive agents increases the risk of developing hypotension.

Thiothixene: (Moderate) Thiothixene should be used cautiously in patients receiving antihypertensive agents. Additive hypotensive effects are possible.

Timolol: (Moderate) Epoprostenol can have additive effects when administered with other antihypertensive agents, including beta-blockers. These effects can be used to therapeutic advantage, but dosage adjustments may be necessary.

Tinzaparin: (Moderate) When used concurrently with anticoagulants, epoprostenol may increase the risk of bleeding.

Tizanidine: (Moderate) Concurrent use of tizanidine with antihypertensive agents can result in significant hypotension. Caution is advised when tizanidine is to be used in patients receiving concurrent antihypertensive therapy.

Tolmetin: (Moderate) NSAIDs may decrease the effect of antihypertensive agents through various mechanisms, including renal and peripheral vasoactive pathways.

Trandolapril; Verapamil: (Moderate) Calcium-channel blockers can have additive hypotensive effects with other antihypertensive agents. This additive effect can be desirable, but the patient should be monitored carefully and the dosage should be adjusted based on clinical response.

Tranylcypromine: (Moderate) Additive hypotensive effects may be seen when MAOIs are combined with antihypertensives or medications with hypotensive properties. Careful monitoring of blood pressure is suggested during concurrent therapy of MAOIs with epoprostenol.

Trazodone: (Minor) Due to additive hypotensive effects, patients receiving antihypertensive agents concurrently with trazodone may have excessive hypotension. Decreased dosage of the antihypertensive agent may be required when given with trazodone.

Treprostinil: (Moderate) Treprostinil can enhance the hypotensive effects of antihypertensive agents or diuretics if given concomitantly. This additive effect may be desirable, but dosages must be adjusted accordingly.

Urea: (Moderate) Further reductions in blood pressure may occur when epoprostenol is administered with diuretics.

Valdecoxib: (Moderate) NSAIDs may decrease the effect of antihypertensive agents through various mechanisms, including renal and peripheral vasoactive pathways.

Valsartan: (Moderate) Angiotensin II receptor antagonists can enhance the hypotensive effects of antihypertensive agents if given concomitantly. This additive effect may be desirable, but dosages must be adjusted accordingly.

Valsartan; Hydrochlorothiazide, HCTZ: (Moderate) Angiotensin II receptor antagonists can enhance the hypotensive effects of antihypertensive agents if given concomitantly. This additive effect may be desirable, but dosages must be adjusted accordingly.

Vasodilators: (Major) Further reductions in blood pressure may occur when vasodilators are combined with epoprostenol.

Verapamil: (Moderate) Calcium-channel blockers can have additive hypotensive effects with other antihypertensive agents. This additive effect can be desirable, but the patient should be monitored carefully and the dosage should be adjusted based on clinical response.

Warfarin: (Moderate) When used concurrently with anticoagulants, epoprostenol may increase the risk of bleeding.

Yohimbine: (Moderate) Yohimbine can increase blood pressure and therefore can antagonize the therapeutic action of antihypertensive agents. Use with particular caution in hypertensive patients with high or uncontrolled BP.

Ziprasidone: (Minor) Ziprasidone is a moderate antagonist of alpha-1 receptors and may cause orthostatic hypotension with or without tachycardia, dizziness, or syncope. Additive hypotensive effects are possible if ziprasidone is used concurrently with antihypertensive agents.

PREGNANCY AND LACTATION

Pregnancy

Pregnant women with untreated pulmonary arterial hypertension are at risk for heart failure, stroke, preterm delivery, and maternal and fetal death. Limited published data from case series and case reports have not established an association with epoprostenol and major birth defects, miscarriage or adverse maternal or fetal outcomes when epoprostenol is used during pregnancy. No evidence of impaired fertility or harm to the fetus have been observed at doses 2.5 times the recommended human dose in rats and 4.8 times the recommended human dose based on BSA in rabbits. It is not known if epoprostenol crosses the placenta; however, because it is rapidly hydrolyzed in the plasma after administration, it is unlikely that the fetus would be exposed to a clinically significant amount of drug. In addition, epoprostenol is a naturally-occurring prostaglandin in the fetus, and therefore, it is unlikely that maternal administration would result in direct adverse effects on the fetus or embryo. There is limited experience with the use of epoprostenol in the treatment of severe pre-eclampsia. Fetal bradycardia, fetal heart rate decelerations, and death were reported and were not attributed to the drug but rather to the severity of the disease in the mother. In addition, administration did not result in changes in maternal pulse, fetal pulse rate, or uterine contractility in a study of 13 women with either superimposed preeclampsia or preeclampsia. There was also no change in placental or fetal blood flow. Epoprostenol has also been used in pregnant women with pulmonary hypertension. One woman was successfully treated with both IV and inhaled epoprostenol with no adverse effects reported on the infant. In another case report, 3 women with pulmonary arterial hypertension received epoprostenol throughout their pregnancy and delivered with no adverse effects noted in the infants. The authors concluded that its use in stable patients may enable successful completion of pregnancy, but caution that pregnancy in women with pulmonary hypertension poses high risk to both the mother and child and should be avoided.

There are no data on the presence of epoprostenol in either human or animal milk, the effects on the breast-fed infant, or the effect on milk production. Consider the developmental and health benefits of breast-feeding along with the mother's clinical need for epoprostenol and any potential adverse effects on the breast-fed child from epoprostenol or the underlying maternal condition. However, because it is rapidly degraded at physiologic pH and probably in the gut, it is unlikely that a clinically significant amount of drug would be excreted into breast milk and available for exposure to a breast-feeding infant. In addition, inhaled epoprostenol has been administered directly to a premature neonate with beneficial effects. Consider the benefits of breast-feeding, the risk of potential infant exposure, and the risk of an untreated or inadequately treated condition. If a breast-feeding infant experiences an adverse effect related to a maternally ingested drug, health care providers are encouraged to report the adverse effect to the FDA.

MECHANISM OF ACTION

The actions of epoprostenol, vasodilation of pulmonary and systemic arterial vascular beds, and platelet aggregation, are in direct opposition to thromboxane A₂, another prostaglandin. The inhibitory action of epoprostenol on platelet aggregation is mediated by the stimulation of adenylate

cyclase and subsequent increase in cyclic AMP in platelets. Hemodynamic effects of epoprostenol are due to increases in cyclic AMP in vascular smooth muscle and subsequent vasodilation. The hemodynamic effects of epoprostenol include decreased pulmonary vascular resistance, increased cardiac index, and increased oxygen delivery. Hypotension, however, is also a hemodynamic effect.

PHARMACOKINETICS

Epoprostenol is administered intravenously. However, it has also been used for inhalation successfully in the treatment of primary pulmonary hypertension. Epoprostenol is rapidly hydrolyzed at neutral pH in blood and also subject to enzymatic degradation. Epoprostenol is extensively metabolized. It is metabolized to 2 primary metabolites, both of which have pharmacological activity of orders of magnitude less than epoprostenol in animal studies, and 14 additional minor metabolites have been isolated from urine. After tritium-labeled epoprostenol administration to humans, the recovery of radioactivity in urine and feces over 1 week was 82% and 4% of the administered dose, respectively. The in vitro half-life of epoprostenol in human blood at 37 degrees C and pH of 7.4 is approximately 6 minutes; therefore, the in vivo half-life of epoprostenol is expected to be no more than 6 minutes.

Intravenous Route

Hemodynamic changes due to epoprostenol returned to baseline within 10 minutes of ending 60-minute intravenous infusions of 1 to 16 ng/kg/minute.