

Patient Profile for Biltmore, Gerald

General Information

ID: gb04052011
Prescriber: Haistings, Ivan M.D.
Name: Biltmore, Gerald
Address: 110 Marion Street
City: Fayetteville
State: GA
Zip: 30224
Country: USA
Phone: 770,345,5436 Daughter 770.456.3456

Current Conditions

- angina
 - edema
 - heart failure
 - hypertension
 - nutritional supplementation
 - osteoarthritis in left hip
 - renal impairment
 - TURP
 - urticaria
-

Current Allergies

No allergies noted

Current Medications

- Medication
 - Advanced Artery Solution Vitamin Sig daily
 - Coenzyme Q10 Sig: twice a day
 - Digoxin Dosage: 0.125mg Sig: daily
 - Isosorbide Mon. Dosage: 30mg ER Sig: daily
 - Lasix® Dosage: 40mg Sig: daily
 - Liver & Kidney Vitamins Sig: daily
 - Metoprolol Dosage: 25mg Sig: twice a day
 - Nifedical™ XL Dosage: 30mg Sig: daily
 - Ocuville® PreserVision(like vitamin) Sig: three times a day
 - Therapeutic Multivitamin/Minerals Sig: three times a day
-

Dosing Parameters

Gender: Male
Birthdate: 11/11/1911
Weight: 58.64 kgs
Height: 167.64 cm
Ideal Body Weight: 64.64 kgs
Body Surface Area: 1.65 m²
Serum Creatinine: 1 mg/dL
Creatinine Clearance: 33.39 mL/min

Notes

Title: Initial Interview & Assessment

Date: 04/05/2011

This 99 year old white male presents with a large bag of prescription and nutraceuticals that he takes on a regular basis. His doctor referred him to me to evaluate the need for all of these drugs. It was inspiring to talk to him and marvel over his very sharp and clear cognitive abilities as well as his physical condition. He has a sister who is 91 and another that is 97 who live close by and he was accompanied on our visit today by his 77 year old daughter. I do not have any laboratory work to evaluate but will ask his doctor to run the necessary laboratory tests to give us a base line to evaluate in the future. Our discussion showed that he had a high confidence level in all the nutraceuticals he is currently taking and attributes his age and condition to these products. Although some are good, possibly taken to excess, the Multivitamin with Minerals and the Vitamin product with beta carotene, Lutein and zeaxantin the three pigments needed in the macular of the eye to prevent macular degeneration should be continued at this time. The CoQ10, the Liver & Kidney and the Advanced Artery Solution are just duplicates of multivitamins with a few added other herbal ingredients of which there are no recognized studies to substantiate value in this patient and should be discontinued. He has some type of dermatitis on his legs which may be related to some of these herbal products or either the dihydropyridone (Nifedipine) or beta blocker (metoprolol) allergic reactions. The blisters on the patient's left leg looked more like the symptoms you see with the nifedipine. Additionally, concomitant use of a Nitrate (isosorbide), dihydropyridone (Nifedipine) and beta blocker (metoprolol) is not necessary to support the patient's cardio/hypertensive problems. The patient has had several falls, and I suspect orthostatic hypotension. His age and weight are definite reasons for not using nitrate therapy in this patient. This drug combined with the nifedipine, which is not recommended in the very old, and the beta blocker place the patient at very high risk for serious falls and injury from the orthostatic hypotension. Changing and consolidating these drugs into the use of a benzothiazepine calcium channel blocker is more geriatric friendly and will support all of his needs. Additionally the use of the short half life LOOP diuretic (Lasix) will allow for rebound antidiuretic response which will lead to continued need to increase dosing. Using the 24 hour half life LOOP (Demadex) will not allow for the rebound antidiuretic effects and will allow for continued low dosing. Keeping the glycoside (Lanoxin) is recommended and at the current dose of 0.125mg daily. He has a fear of taking Aspirin and using Fish Oil capsules will provide the antiplatelet inhibition and support his needs. The patient says that the shot the doctor gave him on his last visit has helped his hip which he says sometimes is painful. A PRN order for Tramadol to be used when he has aches and pain will keep him away from OTC NSAID use which could result in fatal GI bleeds. A breakdown of each drug will follow in this report.

Additionally for the physician's analysis and support of each statement made in this report, there are (3) three pages of references to substantiate all findings and recommendations.

Title: Drug Therapy Evaluation & Recommendations

Date: 04/05/2011

Review of the drug therapy currently prescribed resulted in the following problem areas:

Advanced Artery Solution - a multivitamin with several other herbal products included that are not needed and most of the ingredients are duplicated in the multivitamin. This product should be discontinued.

Coenzyme Q10 - the vitamin company told the patient this was good for his heart and he has been taking it for years. No credible studies substantiate this claim. This product should be discontinued.

Lanoxin - an old cardiac glycoside that still has use in heart health. Since his creatinine clearance could not be calculated due to lack of lab work, I calculated an approximate CrCl of about 30cc/min. With this value dosing of Lanoxin should not exceed 0.125mg even though Dig levels may run low at this dose the effects will still be therapeutic and beneficial.

Isosorbide - nitrate use in the very old is not recommended. Elderly patients may be more sensitive to the hypotensive effects of nitrates. The elderly are at higher risk of falling due to syncope at therapeutic doses of nitrates. Elderly patients may have reduced baroreceptor function; severe orthostatic hypotension may occur when vasodilators such as nitrates are administered. Nitrate therapy can also worsen angina due to hypertrophic cardiomyopathy, particularly in the elderly. Changes to the benzothiazepine ccb (Diltiazem CD) will resolve this problem.

Lasix - the LOOP diuretic that has a short half life is satisfactory when use is short term of immediate response is needed. A long half life (24 hours) of the torsemide (Demadex) is the choice for long term use.

Liver & Kidney Formula - again, multiple duplications of the vitamins listed in the multivitamin and the addition of some other herbal products that claim to do unsubstantiated tasks make continued use not recommended. If the patient needs some help in maintaining regularity of bowel movements, a stool softener will provide the support without all the excess vitamins.

Metoprolol - the use of beta blockers in the geriatric is not recommended. Metoprolol is primarily metabolized by cytochrome P450 2D6. The rate of metabolism is dependent partly on the genetic polymorph that determines the rate of hepatic hydroxylation. About 40% of Caucasian livers do not produce CYP 2D6 after age 60, therefore the desired effects of the drug are unpredictable. Although the desired outcomes are not always produced, the adverse events are still active and ongoing. Since the patient suffers from some type of allergic dermatitis the beta blocker is also suspect. Dermatologic reactions with beta-blockers are usually mild and transient. Some of these reactions include rash (unspecified), pruritus, skin hyperpigmentation, reversible alopecia, and xerosis. Urticaria and worsening of psoriasis have also been reported. Exfoliative dermatitis is reported following therapy with beta-blockers. Rarely, photosensitivity

has been reported during metoprolol therapy. The consolidation to the benzothiazepine ccb (Diltiazem CD) should help resolve this issue.

Nifedical XL - long term nifedipine use is not recommended. Because of the high risk of orthostatic hypotension, use in geriatrics is not recommended. The use of nifedipine immediate-release dosage forms in elderly (aged ≥ 71 years) for the treatment of hypertension has been associated with a nearly 4-fold increase in risk for all-cause mortality when compared to other antihypertensives (beta-blockers, ACE inhibitors, or non-dihydropyridine (benzothiazepine) calcium channel blockers). Exfoliative dermatitis, erythema multiforme, Stevens-Johnson syndrome, and toxic epidermal necrolysis have been reported. Nifedipine has also been associated with acute generalized exanthematous pustulosis (AGEP). Therefore removal of this suspect is advised.

PreserVision like vitamins for eyes - this product contains the essential Beta Carotene, Lutein and zeaxanthin pigments necessary for prophylaxis of macular degeneration. He takes them three times a day which provides high amounts of these three pigments which most studies recommend. Although the Zinc, Copper, and a few other minerals are inconsistent with his renal clearance, the amounts should be safe for him to continue his current regimen. I am including some of the recent data for review.

Therapeutic Multivitamin/Minerals - this formulation is very similar to the Centrum Silver formulation and continued use is recommended. Currently he is taking one tablet three times a day and this should be reduced to daily.

Drug Therapy Management

Stop the following drugs:

Stop: Advanced Artery Solution Vitamins

Stop: Coenzyme Q10

Stop: Isosorbide ER 30mg (following tapering instruction listed with Diltiazem CD)

Stop: Lasix 40mg

Stop: Liver & Kidney Vitamins

Stop: Metoprolol 25mg (following tapering instructions listed with Diltiazem CD)

Stop: Nifedical XL 30mg

New Drug Therapy

Start or continue the following drugs:

Digoxin 0.125mg each morning

Diltiazem CD 120mg daily

Taper to Discontinue: Isosorbide ER 30mg every other morning for 5 doses and Stop completely

Taper to Discontinue: Metoprolol 25mg every morning for 4 doses then every other morning for 4 doses and Stop Completely.

Torsemide (Demadex) 10mg each morning for water pill

Fish Oil 1200mg or Flaxseed three times a day

Eye Health Vision Vitamins tablet 1 three times a day

MegaVitamin with Minerals tablet 1 each morning

Tramadol 50mg tablet 1 every 12 hours ONLY IF NEEDED FOR PAIN

Laboratory Test Needed for Baseline:

Serum Digoxin

TSH

CMP

CBC

HGA1c

Please have the doctor FAX the results to my office

Remember that it will take time to see all the changes that the new drug therapy will produce. After completing the titration processes that are required, we should see big improvements relating to the complaints recorded. The reduction of some of the vitamin supplements should also make you feel better after 30 days or so. Further titration of the diltiazem dosing may be needed until we reach your dose. Continue to keep your blood pressure and pulse log if you can get the nurse at the apartment complex to take and record at least twice a week and report the results to me weekly. This is very important. Using the Demadex for fluid control should be more comfortable and provide you with a constant control of fluid buildup. Remember that you only need to take the MegaVitamin with Minerals once a day (each morning). Taking them more than that will not provide any more benefits to you or your health. Getting the doctor to do the suggested lab work will give us a baseline to follow in the future.

It is very important that we stay in touch. With this in mind I would like for you to call me if you experience any problems anytime and at least weekly to share your blood pressure and pulse values with me. These follow up calls are included in your initial fee and no further charges are placed on you until after our July visit. Please call in June and make an appointment for some time in July.

Let me remind you that this drug therapy regimen is thoroughly thought out and should be followed in its entirety. Choosing only bits and pieces of it may keep us from reaching our mutual goal of improvement in your quality of life and health. I am as close as your phone, so if problems occur please call me. *I look forward to seeing you for a follow-up visit around the end of June or the first of July but would like a progress report weekly by phone until we have all your medication dosages adjusted for you.*

Additionally a computerized analysis of the patient's current drug therapy accompanies this report with attached references for all areas of drug therapy.

Drug Interactions

Digoxin and Furosemide (Lasix®)

 Severity: [Moderate](#)

Since electrolyte disorders modify the actions of digoxin, drugs that can affect electrolyte balance potentially can affect the response to digoxin. Hypokalemia, hypomagnesemia, or hypercalcemia increase digoxin's effect.[\[4999\]](#) The following drugs can precipitate digoxin toxicity via their effect on electrolyte balance: amphotericin B [\[5062\]](#), corticosteroids [\[6115\]](#), corticotropin, ACTH, potassium-depleting diuretics (e.g., acetazolamide [\[4994\]](#), loop diuretics [\[3085\]](#), methazolamide [\[5023\]](#), and thiazide diuretics [\[3085\]](#) [\[5219\]](#)), and sodium polystyrene sulfonate [\[6116\]](#). Calcium salts augment the actions of digoxin. In addition, when calcium is administered via rapid intravenous injection, the risk of serious arrhythmias in digitalized patients is increased.[\[4999\]](#) It is recommended that serum potassium, magnesium, and calcium be monitored regularly in patients receiving digoxin.

Electrolyte disturbances (e.g., hypokalemia, hypomagnesemia, hypercalcemia) may occur with administration of loop diuretics, including furosemide.[\[5159\]](#) Hypokalemia increases the potential for proarrhythmic effects (e.g., torsade de pointes) due to arsenic trioxide, cardiac glycosides, dofetilide [\[4947\]](#), or levomethadyl. Potassium levels should be within the normal range prior and during administration of these agents. In the absence of electrolyte imbalances, furosemide and these agents can be used together safely.

Digoxin and Metoprolol

 Severity: [Moderate](#)

Interactions occur between digoxin and a variety of other cardiovascular agents. These can be categorized into two groups: a) pharmacokinetic interactions that reduce the clearance of digoxin and may lead to digoxin toxicity: amiodarone [\[5802\]](#), felodipine [\[5827\]](#), diltiazem [\[5802\]](#), propafenone [\[5001\]](#) [\[5014\]](#), quinidine [\[5802\]](#), and verapamil [\[5802\]](#); and b) pharmacodynamic interactions that may potentiate the actions of digoxin: amiodarone, dofetilide, sotalol, beta-blockers [\[5001\]](#), diltiazem, and verapamil. Digoxin is a substrate for P-glycoprotein.[\[4718\]](#) Quinidine and verapamil inhibit P-glycoprotein, an energy-dependent cellular drug efflux pump. The inhibition of p-glycoprotein in the intestinal cell wall may lead to increased oral absorption of digoxin; however, it has been shown that both quinidine and verapamil inhibit the secretion of digoxin by p-glycoprotein transporters in the kidney leading to decreased renal tubular elimination of digoxin and increased serum concentrations.[\[6114\]](#) It has been recommended that digoxin doses be reduced by 50% when adding quinidine therapy, and serum digoxin levels closely monitored thereafter.[\[5001\]](#) Despite potential for interactions, digoxin sometimes is intentionally used in combination with a beta-blocker, diltiazem, or verapamil to further reduce conduction through the AV node. Nevertheless, these combinations should be used cautiously, and digoxin dosages may need adjustment in some patients.[\[4999\]](#)

Because the pharmacologic effects of metoprolol include AV nodal conduction depression,[\[5269\]](#) additive effects are possible when used with other antiarrhythmics, that exert significant effects on AV nodal conduction including, adenosine [\[5001\]](#), cardiac glycosides [\[4999\]](#), disopyramide [\[4954\]](#), or other antiarrhythmics or drugs that significantly depress AV nodal conduction. When used with beta-blockers, these agents can cause AV block and bradycardia. Additionally, using metoprolol with sotalol would be illogical as both are beta-blockers and would represent duplicate therapy; additive effects on AV nodal conduction and blood pressure would be expected.[\[5001\]](#) Bretylium is associated with hypotension [\[2999\]](#) and should be used cautiously in patients receiving other drugs known to cause hypotension including beta-blockers.

Digoxin and Calcium Salts (found in Therapeutic Multivitamin with Minerals)

 Severity: [High](#)

Since electrolyte disorders modify the actions of digoxin, drugs that can affect electrolyte balance potentially can affect the response to digoxin. Hypokalemia, hypomagnesemia, or hypercalcemia increase digoxin's effect.[\[4999\]](#) The following drugs can precipitate digoxin toxicity via their effect on electrolyte balance: amphotericin B [\[5062\]](#), corticosteroids [\[6115\]](#), corticotropin, ACTH, potassium-depleting diuretics (e.g., acetazolamide [\[4994\]](#), loop diuretics [\[3085\]](#), methazolamide [\[5023\]](#), and thiazide diuretics [\[3085\]](#) [\[5219\]](#)), and sodium polystyrene sulfonate [\[6116\]](#). Calcium salts augment the actions of digoxin. In addition, when calcium is administered via rapid intravenous injection, the risk of serious arrhythmias in digitalized patients is increased.[\[4999\]](#) It is recommended that serum potassium, magnesium, and calcium be monitored regularly in patients receiving digoxin.

Intravenous administration of calcium should particularly be avoided in patients taking cardiac glycosides [\[4999\]](#) due to an increased risk of developing arrhythmias. Calcium and cardiac glycosides are synergistic in their inotropic and chronotropic effects and

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hypocalcemia can compromise the therapeutic actions of digitalis. [227] Cardiac glycoside therapy, however, does not preclude the use of calcium salts. Nevertheless, arrhythmias can occur if the calcium salts are given IV to patients on cardiac glycosides. The manufacturer recommends that PhosLo® (calcium acetate), indicated for treating hyperphosphatemia, should not be coadministered to patients receiving digoxin to avoid the risk of hypercalcemia and associated cardiac arrhythmias.

Digoxin and Nifedipine (Nifedical™ XL)

⚠Severity: [Moderate](#)

Digoxin serum concentrations may be increased by up to 45% by concomitant administration of nifedipine. [5802] This is believed to be due to decreased renal and nonrenal clearance of digoxin by nifedipine. Despite some reports showing no effect on digoxin, plasma levels of digoxin should be monitored carefully when nifedipine is administered.

Digoxin and Magnesium Salts (found in Therapeutic Multivitamin with Minerals)

⚠Severity: [High](#)

Magnesium salts, such as magnesium sulfate, can antagonize the electrophysiologic effects of digoxin. Nevertheless, it is acceptable to administer magnesium salts to patients in order to achieve appropriate serum magnesium concentrations. [6127] Magnesium has also been shown to be an effective adjunct in the treatment of digoxin-induced arrhythmias. [6128]

Magnesium salts, such as magnesium sulfate, can antagonize the electrophysiologic effects of digoxin or other cardiac glycosides. Nevertheless, it is acceptable to administer magnesium salts to patients in order to achieve appropriate serum magnesium concentrations. [6127] Magnesium has also been shown to be an effective adjunct in the treatment of digoxin-induced arrhythmias. [251] [252] [6128] [7197] [7207] However, concurrent use of digoxin or other cardiac glycosides with oral magnesium citrate may inhibit absorption and possibly decrease plasma concentrations of the glycoside. [4999] Saline laxatives such as magnesium citrate must be administered with caution to patients receiving cardiac glycoside therapy as electrolyte disturbances, particularly hypokalemia, are possible with their use. Cardiac conduction changes and heart block may occur in patients with electrolyte imbalances. [6115]

Isosorbide Mononitrate and Furosemide (Lasix®)

⚠Severity: [Moderate](#)

Concomitant use of isosorbide mononitrate with other antihypertensive agents, peripheral vasodilators, beta-blockers, opiate agonists, phenothiazines, or ethanol (moderate or excessive amounts) [5944] can cause additive hypotensive effects. [6288] Marked orthostatic hypotension has been reported following the concomitant administration of calcium-channel blockers and organic nitrates, and dosage adjustments may be necessary. [6288]

Isosorbide Mononitrate and Metoprolol

⚠Severity: [Moderate](#)

Concomitant use of isosorbide mononitrate with other antihypertensive agents, peripheral vasodilators, beta-blockers, opiate agonists, phenothiazines, or ethanol (moderate or excessive amounts) [5944] can cause additive hypotensive effects. [6288] Marked orthostatic hypotension has been reported following the concomitant administration of calcium-channel blockers and organic nitrates, and dosage adjustments may be necessary. [6288]

Isosorbide Mononitrate and Nifedipine (Nifedical™ XL)

⚠Severity: [Moderate](#)

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Furosemide (Lasix®) and Metoprolol

⚠Severity: [Moderate](#)

Additive hypotension is possible if furosemide used in combination with any other antihypertensive agents, [5159] including drugs such as nitroglycerin. Hyponatremia or hypovolemia predisposes patients to acute hypotensive episodes following initiation of ACE inhibitor therapy. While ACE inhibitors and loop diuretics are routinely administered together in the treatment of heart failure, if an ACE inhibitor is to be administered to a patient receiving furosemide, initial doses should be conservative.

Metoprolol is an antihypertensive agent, so its effects are additive with other antihypertensive agents. [6714] This interaction is often used advantageously in treating hypertension; however, lower doses of each agent may be necessary. Hypotension can be potentiated when beta-blockers are co-administered with dihydropyridine-type calcium-channel blockers, most notably rapid-release nifedipine. Nifedipine has been reported to increase plasma concentrations and oral bioavailability of certain beta-blockers (e.g., metoprolol, propranolol). It is prudent to avoid using beta-blockers with guanethidine, reserpine, or other rauwolfia alkaloids that have a high incidence of orthostatic hypotension due to catecholamine depletion, since beta-blockers will interfere with reflex tachycardia, worsening the orthostasis. [5269]

Furosemide (Lasix®) and Nifedipine (Nifedical™ XL)

⚠️ Severity: [Moderate](#)

Additive hypotension is possible if furosemide used in combination with any other antihypertensive agents, [5159] including drugs such as nitroglycerin. Hyponatremia or hypovolemia predisposes patients to acute hypotensive episodes following initiation of ACE inhibitor therapy. While ACE inhibitors and loop diuretics are routinely administered together in the treatment of heart failure, if an ACE inhibitor is to be administered to a patient receiving furosemide, initial doses should be conservative.

Nifedipine can have additive hypotensive effects with alpha-blockers and other antihypertensive agents (including diuretics). [5803] This additive effect can be desirable, but the patient should be monitored carefully and the dosage should be adjusted based on clinical response. In addition to potential additive hypotensive effects, diltiazem has been reported to increase the plasma level and hypotensive effects of nifedipine and amlodipine via CYP3A4 inhibition. [5804] Verapamil may also inhibit CYP3A4 metabolism of nifedipine. The concomitant use of dihydropyridine calcium-channel blockers and beta-blockers can reduce angina and improve exercise tolerance. When these drugs are given together, however, hypotension and impaired cardiac performance can occur, especially in patients with left ventricular dysfunction, cardiac arrhythmias, or aortic stenosis. [5803]

Metoprolol and Nifedipine (Nifedical™ XL)

⚠️ Severity: [Moderate](#)

Metoprolol is an antihypertensive agent, so its effects are additive with other antihypertensive agents. [6714] This interaction is often used advantageously in treating hypertension; however, lower doses of each agent may be necessary. Hypotension can be potentiated when beta-blockers are co-administered with dihydropyridine-type calcium-channel blockers, most notably rapid-release nifedipine. Nifedipine has been reported to increase plasma concentrations and oral bioavailability of certain beta-blockers (e.g., metoprolol, propranolol). It is prudent to avoid using beta-blockers with guanethidine, reserpine, or other rauwolfia alkaloids that have a high incidence of orthostatic hypotension due to catecholamine depletion, since beta-blockers will interfere with reflex tachycardia, worsening the orthostasis. [5269]

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In general, concomitant therapy of nifedipine with beta-blockers is well tolerated and can even be beneficial in some cases (i.e., inhibition of nifedipine-induced reflex tachycardia by beta-blockade). Negative inotropic and/or chronotropic effects can be additive when these drugs are used in combination. Finally, angina has been reported when beta-adrenergic blocking agents are withdrawn abruptly and nifedipine therapy is initiated. A gradual downward titration of the beta-adrenergic blocking agent dosage during initiation of nifedipine therapy may minimize or eliminate this potential interaction. [5803] Hypotension and impaired cardiac performance can occur during coadministration of nifedipine with beta-blockers, especially in patients with left ventricular dysfunction, cardiac arrhythmias, or aortic stenosis. [5803] Monitor clinical response during coadministration; adjust of nifedipine dosage may be needed during concurrent beta-blocker therapy. [8552]

Nifedipine (Nifedical™ XL) and Calcium Salts (found in Therapeutic Multivitamin with Minerals)

⚠️ Severity: [Low](#)

Calcium salts are used in the treatment of calcium channel blocker overdose. [5801] In general, high doses of calcium salts are needed to overcome the hypotensive effects of calcium channel blocker overdose. However, the exogenous administration of intravenous calcium salts in non-overdose situations may attenuate the pharmacodynamic response to calcium-channel antagonists. If patients receive intravenous calcium salts during concomitant calcium channel blocker therapy, therapeutic response should be monitored.

Nifedipine (Nifedical™ XL) and Magnesium Salts (found in Therapeutic Multivitamin with Minerals)

⚠️ Severity: [High](#)

Clinically significant drug interactions including neuromuscular blockade and hypotension have occurred when IV magnesium salts were given concurrently with nifedipine during the treatment of hypertension or premature labor during pregnancy. [\[5813\]](#) [\[5814\]](#) The women affected presented with either pronounced muscle weakness and/or hypotension. The effects have been attributed to nifedipine potentiation of the neuromuscular blocking effects of magnesium. It is recommended that nifedipine not be given concurrently with magnesium therapy for pre-eclampsia, hypertension, or tocolytic treatment during pregnancy.

Clinically significant drug interactions including neuromuscular blockade and hypotension have occurred when IV magnesium salts were given concurrently with nifedipine during the treatment of hypertension or premature labor during pregnancy. The women affected presented with either pronounced muscle weakness and/or hypotension. In a few cases, fetal harm was noted as a result of the hypotensive episodes. The effects have been attributed to nifedipine potentiation of the neuromuscular blocking effects of magnesium. It is recommended that nifedipine not be given concurrently with magnesium therapy for pre-eclampsia, hypertension, or tocolytic treatment during pregnancy. [\[5813\]](#)

Beta-Carotene (found in OcuVite® PreserVision®) **and Vitamin A** (found in Therapeutic Multivitamin with Minerals)

⚠️ Severity: [Moderate](#)

Beta-carotene fulfills the requirements for vitamin A supplementation. [\[6957\]](#) Administration of beta-carotene with vitamin A usually is not necessary and should be avoided to prevent the development of hypervitaminosis A. However, if intake of both vitamins remains in the standardly recognized daily allowances for Vitamin A for the individual harmful effects would not be expected.

Ergocalciferol, Vitamin D2 (found in Therapeutic Multivitamin with Minerals) **and Digoxin**

⚠️ Severity: [Moderate](#)

Ergocalciferol should be administered with caution to patients with cardiac disease or those receiving cardiac glycosides. Ergocalciferol may cause hypercalcemia which may affect the actions of the cardiac glycoside and/or lead to cardiac arrhythmias. [\[6916\]](#) [\[4999\]](#)

Magnesium Salts (found in Therapeutic Multivitamin with Minerals) **and Furosemide** (Lasix®)

⚠️ Severity: [Moderate](#)

Diuretics may interfere with the kidneys ability to regulate magnesium concentrations. Long-term use of loop diuretics or thiazide diuretics may impair the magnesium-conserving ability of the kidneys and lead to hypomagnesemia. [\[7114\]](#) Conversely, long-term use of potassium-sparing diuretics has been found to increase renal tubular reabsorption of magnesium which may cause hypermagnesemia in patients also receiving magnesium supplements, especially in patients with renal insufficiency.

Niacin, Niacinamide (found in Therapeutic Multivitamin with Minerals) **and Furosemide** (Lasix®)

⚠️ Severity: [Moderate](#)

Clonidine has been shown to inhibit niacin-induced flushing. [\[7631\]](#) This interaction is harmless unless niacin augments the hypotensive actions of clonidine. Finally, clinicians should keep in mind that cutaneous vasodilation induced by niacin may become problematic if high-dose niacin is used concomitantly with other antihypertensive agents. [\[5932\]](#) especially peripheral vasodilators such as epoprostenol, nitrates, calcium-channel blockers, or others, particularly in the setting of acute myocardial infarction, unstable angina, or other acute hemodynamic compromise.

Niacin, Niacinamide (found in Therapeutic Multivitamin with Minerals) **and Metoprolol**

⚠️ Severity: [Moderate](#)

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Niacin, Niacinamide (found in Therapeutic Multivitamin with Minerals) **and Nifedipine** (Nifedical™ XL)

⚠️ Severity: [Moderate](#)

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Adverse Reactions

- abdominal pain (Digoxin | Lasix® | Metoprolol)
- acute generalized exanthematous pustulosis (AGEP) (Lasix® | Nifedical™ XL)
- agranulocytosis (Lasix® | Metoprolol)
- alopecia (Metoprolol)
- amnesia (Metoprolol)
- anemia (Lasix®)
- anorexia (Digoxin | Lasix®)
- anxiety (Digoxin)
- aplastic anemia (Lasix®)
- arthralgia (Metoprolol)
- asthenia (Nifedical™ XL)
- atrial fibrillation (Digoxin)
- atrial tachycardia (Digoxin)
- AV block (Digoxin | Metoprolol)
- azotemia (Lasix®)
- blurred vision (Digoxin | Lasix® | Metoprolol)
- bradycardia (Digoxin | Metoprolol)
- bronchospasm (Metoprolol)
- chest pain (unspecified) (Metoprolol)
- cholestasis (Lasix®)
- confusion (Digoxin | Metoprolol)
- constipation (Digoxin | Lasix® | Metoprolol)
- cyanosis (Isosorbide Mononitrate)
- delirium (Digoxin)
- depression (Digoxin | Metoprolol)
- diabetes mellitus (Metoprolol)
- diaphoresis (Isosorbide Mononitrate)
- diarrhea (Digoxin | Lasix® | Metoprolol)
- dizziness (Digoxin | Lasix® | Isosorbide Mononitrate | Metoprolol | Nifedical™ XL)
- drowsiness (Digoxin | Metoprolol)
- dyspnea (Metoprolol | Nifedical™ XL)
- edema (Nifedical™ XL)
- elevated hepatic enzymes (Metoprolol)
- erythema (Digoxin)
- erythema multiforme (Nifedical™ XL)
- exfoliative dermatitis (Metoprolol | Nifedical™ XL)
- fatigue (Digoxin | Metoprolol | Nifedical™ XL)
- flatulence (Metoprolol)
- flushing (Isosorbide Mononitrate | Nifedical™ XL)
- gingival hyperplasia (Nifedical™ XL)
- glomerulonephritis (Nifedical™ XL)
- gynecomastia (Digoxin | Nifedical™ XL)
- hallucinations (Digoxin | Metoprolol)
- headache (Digoxin | Lasix® | Isosorbide Mononitrate | Metoprolol | Nifedical™ XL)
- hearing loss (Lasix®)
- heart failure (Metoprolol | Nifedical™ XL)
- hepatitis (Metoprolol)
- hypercalciuria (Lasix®)
- hypercholesterolemia (Lasix®)
- hyperglycemia (Lasix® | Metoprolol)
- hyperkalemia (Digoxin)
- hypertriglyceridemia (Lasix® | Metoprolol)
- hyperuricemia (Lasix®)
- hypocalcemia (Lasix®)
- hypochloremia (Lasix®)

- hypoglycemia (Metoprolol)
- hypokalemia (Digoxin | Lasix®)
- hypomagnesemia (Lasix®)
- hyponatremia (Lasix®)
- hypotension (Lasix® | Isosorbide Mononitrate | Metoprolol | Nifedical™ XL)
- hypovolemia (Lasix®)
- impaired cognition (Digoxin)
- impotence (erectile dysfunction) (Digoxin | Metoprolol)
- insomnia (Metoprolol)
- interstitial nephritis (Lasix®)
- jaundice (Lasix® | Metoprolol)
- leukopenia (Lasix®)
- libido decrease (Digoxin | Metoprolol)
- maculopapular rash (Digoxin)
- metabolic alkalosis (Lasix®)
- methemoglobinemia (Isosorbide Mononitrate)
- musculoskeletal pain (Metoprolol)
- myocardial infarction (Nifedical™ XL)
- nausea/vomiting (Digoxin | Lasix® | Isosorbide Mononitrate | Metoprolol)
- nephrolithiasis (Lasix®)
- oliguria (Lasix®)
- orthostatic hypotension (Lasix® | Isosorbide Mononitrate)
- palpitations (Metoprolol | Nifedical™ XL)
- pancreatitis (Lasix®)
- paresthesias (Digoxin | Lasix®)
- peripheral edema (Metoprolol | Nifedical™ XL)
- peripheral vasoconstriction (Metoprolol)
- peripheral vasodilation (Nifedical™ XL)
- photophobia (Digoxin)
- photosensitivity (Lasix® | Metoprolol | Nifedical™ XL)
- polyuria (Lasix®)
- PR prolongation (Digoxin)
- premature ventricular contractions (PVCs) (Digoxin)
- pruritus (Digoxin | Metoprolol)
- psoriasis (Metoprolol)
- psychosis (Digoxin | Metoprolol)
- pyrosis (heartburn) (Metoprolol)
- rash (unspecified) (Metoprolol)
- rhinitis (Metoprolol)
- sinus tachycardia (Digoxin | Isosorbide Mononitrate | Nifedical™ XL)
- skin hyperpigmentation (Metoprolol)
- Stevens-Johnson syndrome (Digoxin | Nifedical™ XL)
- ST-T wave changes (Digoxin)
- syncope (Digoxin | Lasix® | Isosorbide Mononitrate | Metoprolol | Nifedical™ XL)
- thrombocytopenia (Digoxin | Lasix® | Metoprolol)
- tinnitus (Lasix® | Metoprolol)
- tolerance (Isosorbide Mononitrate)
- toxic epidermal necrolysis (Nifedical™ XL)
- urticaria (Metoprolol)
- ventricular tachycardia (Digoxin)
- vertigo (Nifedical™ XL)
- visual impairment (Digoxin)
- weakness (Digoxin | Nifedical™ XL)
- wheezing (Metoprolol)
- xanthopsia (Digoxin)
- xerosis (Metoprolol)

Indication Alerts

Drugs that can be used to treat current conditions:

- Coenzyme Q10 can be used to treat heart failure, and nutritional supplementation
- Digoxin can be used to treat heart failure
- Isosorbide Mononitrate can be used to treat angina
- Lasix® can be used to treat edema, heart failure, hypertension, and renal impairment
- Metoprolol can be used to treat angina, heart failure, and hypertension
- Nifedical™ XL can be used to treat angina, and hypertension
- OcuVite® PreserVision® can be used to treat nutritional supplementation
- Therapeutic Multivitamin with Minerals can be used to treat hypertension, and nutritional supplementation

Conditions not currently being treated:

- osteoarthritis
- urticaria

Precautions

Precaution: Digoxin in hypertension

IV administration of digoxin can transiently increase blood pressure and should be used cautiously in patients with hypertension.

Precaution: Digoxin in renal impairment

Patients with renal disease, such as acute glomerulonephritis, associated with heart failure should use digoxin with caution. Use of a lower daily dose is recommended with appropriate ECG monitoring based on clinical goals and patient conditions. Digoxin should be used with caution in patients with renal impairment including renal failure because 50% of digoxin is eliminated unchanged via the kidneys. Renal impairment reduces the excretion of the drug and can cause toxicity. Dosages should be decreased, and it should be kept in mind that the time required to reach steady-state concentrations can be prolonged in patients with renal failure.

Precaution: Lasix® in heart failure

Patients with ventricular arrhythmias, heart failure, potassium-losing nephropathy, aldosterone excess, or diarrhea should be monitored closely since furosemide-induced hypokalemia can exacerbate these conditions.

Precaution: Lasix® in renal impairment

Furosemide should not be used in *anuria*. It should be used cautiously in any patient with renal disease such as severe renal impairment or renal failure. Drug-induced hypovolemia can precipitate azotemia in these patients. Furosemide is an effective diuretic for many patients with renal impairment. Renal impairment may reduce clearance and warrant the use of higher doses with extended dosing intervals. Furosemide may be less effective in these patients and delayed excretion of drug may increase the risk of toxicity.

Precaution: Metoprolol in heart failure

Because beta-blockers depress conduction through the AV node, metoprolol is contraindicated in patients with *severe bradycardia, sick sinus syndrome, or advanced AV block (second or third-degree AV block)* unless a functioning pacemaker is present. In general, beta-blockers should not be used in patients with *cardiogenic shock, acute pulmonary edema, or decompensated systolic congestive heart failure*, particularly in those with severely compromised left ventricular dysfunction, because the negative inotropic effect of these drugs can further depress cardiac output. In stable patients with heart failure, however, beta-blockers (e.g., metoprolol, bisoprolol, carvedilol) given in low doses have been documented to be beneficial. Beta-blockers have also been used for the treatment of hypertrophic cardiomyopathy. In the treatment of myocardial infarction, beta-blockers are contraindicated in patients with hypotension (SBP < 100 mmHg).

Precaution: Nifedical™ XL in heart failure

Nifedipine should be used cautiously in patients with severe bradycardia. It also should be used cautiously in patients with congestive heart failure (or left ventricular dysfunction) because nifedipine can precipitate or exacerbate heart failure due to its negative inotropic effects, particularly in patients receiving concomitant beta-blocker therapy. The development or worsening of pulmonary edema is a marker for discontinuation of nifedipine. Immediate-release nifedipine is contraindicated in certain coronary artery disease states which include *cardiogenic shock or acute myocardial infarction* (or other acute coronary syndromes such as unstable angina) due to its negative inotropic effects and the reflex sympathetic activation, tachycardia, and hypotension associated with its use. Although immediate-release nifedipine (including sublingual or 'bite and swallow' administration) was frequently used for the treatment of hypertensive urgencies prior to 1995, [689] serious adverse effects have been reported with its use, primarily due to the unpredictable rate and degree of blood pressure lowering. Profound hypotension, myocardial infarction, and death have been reported when immediate-release nifedipine was used to lower blood pressure acutely. Therefore, according to recommendations of the Joint National Committee on Prevention, Detection Evaluation, and Treatment of High Blood Pressure (JNC-VI), nifedipine liquid-filled capsules are contraindicated in the setting of *hypertensive urgency, hypertensive crisis, or hypertensive emergency*. In addition, the routine, sporadic use of nifedipine liquid-filled capsules whenever blood pressure rises above a predetermined level is not considered

appropriate.^[1331] The immediate-release nifedipine dosage form is currently only indicated for the treatment of chronic stable angina or vasospastic angina.

Precaution: OcuVite® PreserVision® in renal impairment

The safe use of beta-carotene in patients with renal disease or hepatic disease has not been established; therefore, beta-carotene should be used with caution in patients with these conditions. Renal impairment may lead to increased beta-carotene concentrations.

Precaution: OcuVite® PreserVision® in renal impairment

Zinc Chloride injection contains aluminum which may reach toxic levels with prolonged administration in patients with renal impairment or renal failure. Neonates of neonatal prematurity are at particular risk for aluminum toxicity following administration of aluminum-containing injectables since they have immature kidneys. Research indicates that patients with renal impairment, including neonates, who receive parenteral aluminum at rates greater than 4-5 mcg/kg/day may accumulate aluminum at levels associated with CNS and bone toxicity. Tissue loading may occur at lower administration rates.

Precaution: Therapeutic Multivitamin with Minerals in renal impairment

Parenteral pyridoxine solutions contain varying concentrations of aluminum. Patients with renal impairment, especially as seen with neonatal prematurity, are at risk of aluminum accumulation which may result in toxicity. Limit intravenous pyridoxine therapy and consider the cumulative aluminum content among all therapies under administration in patients with renal impairment. It is noted that 4-5 mcg/kg/day of IV aluminum leads to accumulation at concentrations associated with CNS and bone toxicity; further, aluminum tissue loading is possible at lesser, but undefined, daily administration rates.^[9771] Aluminum concentration in parenteral solutions can be obtained by direct manufacturer inquiry.

Precaution: Therapeutic Multivitamin with Minerals in renal impairment

Magnesium salts should be used with caution in patients with renal disease, including patients with renal impairment or renal failure. Magnesium salts are renally eliminated, so patients with renal impairment have an increased risk of developing magnesium toxicity from decreased excretion of magnesium. In patients with severe renal dysfunction, no more than 20 grams (162 mEq) of magnesium should be administered within a 48-hour period. Parenteral magnesium should be avoided in patients with a creatinine clearance of less than 20 mL/minute. Up to 30% of an orally administered dose is absorbed systemically.

Precaution: Therapeutic Multivitamin with Minerals in angina

Due to its vasodilatory action, nicotinic acid (niacin) should be used with caution in those patients with uncorrected hypotension (or predisposition to orthostatic hypotension), acute myocardial infarction, or unstable angina, particularly when vasodilator medications such as nitrates, calcium channel blockers, or adrenergic blocking agents are coadministered (see Drug Interactions). Because the vasodilatory response to niacin may be more dramatic at the initiation of treatment, activities requiring mental alertness (e.g., driving or operating machinery) should not be undertaken until the response to niacin is known.

Precaution: Therapeutic Multivitamin with Minerals in renal impairment

Use niacin with caution in patients with renal disease (renal failure or severe renal impairment) since niacin metabolites are excreted through the kidneys. It appears that no special precautions are needed when administering niacin to meet the recommended nutritional daily allowance (RDA). Use caution when administering higher dosages.

Precaution: Therapeutic Multivitamin with Minerals in renal impairment

Zinc Chloride injection contains aluminum which may reach toxic levels with prolonged administration in patients with renal impairment or renal failure. Neonates of neonatal prematurity are at particular risk for aluminum toxicity following administration of aluminum-containing injectables since they have immature kidneys. Research indicates that patients with renal impairment, including neonates, who receive parenteral aluminum at rates greater than 4-5 mcg/kg/day may accumulate aluminum at levels associated with CNS and bone toxicity. Tissue loading may occur at lower administration rates.

Precaution: Therapeutic Multivitamin with Minerals in renal impairment

Chromium elimination may be decreased in patients with renal disease or renal impairment. Dosage reductions in supplemental parenteral or oral doses may be needed. Since chromium is primarily excreted via the renal route, supplementation should be approached with caution, particularly in patients maintained on dialysis or with renal failure.

Precaution: Therapeutic Multivitamin with Minerals in renal impairment

Selenium supplements should be used cautiously in patients with GI disease or renal impairment. These conditions may cause high levels of selenium; dosage reductions may be necessary.

Allergy Alerts

No warnings noted

References

227. Chopra D, Janson P, Sawin CT. Insensitivity to digoxin associated with hypocalcemia. *N Engl J Med* 1977;296:917-8.
251. French JH, Thomas RG, Siskind AP et al. Magnesium therapy in massive digoxin intoxication. *Ann Emerg Med* 1984;13:562-6.
252. Spector MJ, Schweizer E, Goldman RH. Studies on magnesium's mechanism of action in digitalis-induced arrhythmias. *Circulation* 1975;52:1001-5.
689. Gifford RW. Management of hypertensive crises. *JAMA* 1991;266:829-35.
1331. Grossman E, Messerli FH, Grodzicki T et al. Should a moratorium be placed on sublingual nifedipine capsules given for hypertensive emergencies and pseudoemergencies? *JAMA* 1996;276:1328-31.
2999. Guidelines 2000 for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. Part 6: advanced cardiovascular life support. *Circulation* 2000;102(8 Suppl):112-165.
3085. Cohn JN, Kowey PR, Whelton PK, Prisant LM. New guidelines for potassium replacement in clinical practice: a contemporary review by the National Council on Potassium in Clinical Practice. *Arch Intern Med* 2000;160:2429-36.
4718. Hansten PD, Horn JR. Cytochrome P450 Enzymes and Drug Interactions, Table of Cytochrome P450 Substrates, Inhibitors, Inducers and P-glycoprotein, with Footnotes. In: *The Top 100 Drug Interactions - A guide to Patient Management*. 2008 Edition. Freeland, WA: H&H Publications; 2008:142-157.
4947. Tikosyn™ (dofetilide) package insert. New York, NY: Pfizer Labs; 1999 Dec.
4954. Norpace® (disopyramide) package insert. Chicago, IL: GD Searle LLC; 2001 Sept.
4994. Acetazolamide package insert. Danbury, CT: Danbury Pharmaceutical; 1998 April.
4999. Lanoxin® (digoxin) package insert. Research Triangle Park, NC: Glaxo Smith Kline; 2001 Aug.
5001. Trujillo TC, Nolan PE. Antiarrhythmic agents: drug interactions of clinical significance. *Drug Saf* 2000;23:509-32.
5014. Rythmol® SR (propafenone hydrochloride) package insert. North Chicago, IL: Abbott Laboratories, Inc.; 2006 Jan.
5023. Neptazane® (methazolamide) package insert. Pearle River, NY: Lederle Pharmaceutical Division; 1998 Nov.
5062. Amphocin® (amphotericin B) package insert. Kalamazoo, MI: Pharmacia Corporation; 2003 Sep.
5159. Lasix® (furosemide) package insert. Bridgewater, NJ: Aventis Pharmaceuticals; 2004 Jan.
5219. Shapiro, S., et al. The epidemiology of digoxin, a study in three Boston hospitals. *J Chron Dis* 1969; 22:361.
5269. Toprol-XL® (metoprolol succinate) package insert. Wilmington, DE: AstraZeneca Pharmaceuticals LP; 2007 Jul.
5801. Salhanick SD, Shannon MW. Management of calcium channel antagonist overdose. *Drug Safety* 2003;26:65-79.
5802. Rodin SM, Johnson BF. Pharmacokinetic interactions with digoxin. *Clin Pharmacokin* 1988;227-44.
5803. Procardia® (nifedipine) package insert. New York, NY: Pfizer Labs, Inc.; 2003 Sep.

- 5804.** Ohashi K, Tateishi T, Sudo T, et al. Effects of diltiazem on the pharmacokinetics of nifedipine. *J Cardiovasc Pharmacol* 1990;15:96-101.
- 5813.** Snyder SW, Cardwell MS. Neuromuscular blockade with magnesium sulfate and nifedipine. *Am J Obstet Gynecol* 1989;161:35-6.
- 5814.** Waisman GD, Mayorga LM, Camera MI, et al. Magnesium plus nifedipine: potentiation of hypotensive effect in preeclampsia? *Am J Obstet Gynecol* 1988;159:308-9.
- 5827.** Rehnqvist N, Billing E, Moberg L, et al. Pharmacokinetics of felodipine and effect on digoxin plasma levels in patients with heart failure. *Drugs* 1987;34 Suppl 3:33-42.
- 5932.** Niaspan® (niacin extended-release tablets) Miami, FL: Kos Pharmaceuticals, Inc; 2003 July.
- 5944.** Johnson RH, Eisenhofer G, Lambie DG. The effects of acute and chronic ingestion of ethanol on the autonomic nervous system. *Drug Alcohol Depend* 1986;18:319-28.
- 6114.** Lin JH, Yamazaki M. Role of p-glycoprotein in pharmacokinetics: clinical implications. *Clin Pharmacokinet* 2003;42:59-98.
- 6115.** Nanji AA. Drug-induced electrolyte disorders. *Drug Intell Clin Pharm* 1983;17:175-85.
- 6116.** Kayexalate (sodium polystyrene sulfonate) package insert. New York, NY: Sanofi-Synthelabo, Inc.; 1999 Sep.
- 6127.** Douban S, Brodsky MA, Whang DD. Significance of magnesium in congestive heart failure. *Am Heart J* 1996;132:664-71.
- 6128.** Kinlay S, Buckley NA. Magnesium sulfate in the treatment of ventricular arrhythmia due to digoxin toxicity. *J Toxicol Clin Toxicol* 1995;33:55-9.
- 6288.** Imdur® (isosorbide mononitrate) package insert. Kenilworth, NJ: Key Pharmaceuticals; 2002 Jul.
- 6714.** Lam YWF, Shepherd AMM. Drug interactions in hypertensive patients: pharmacokinetic, pharmacodynamic, and genetic considerations. *Clin Pharmacokinet* 1990;18:295-317.
- 6916.** Drisdol® (ergocalciferol) package insert. New York, NY: Sanofi-Synthelabo, Inc.; 2003 Dec.
- 6957.** Standing Committee on the Scientific Evaluation of Dietary Reference Intakes-Panel on Micronutrients and the Subcommittee on Upper Reference Levels of Nutrients, Food and Nutrition Board, Institute of Medicine (IOM). *Dietary Reference Intakes for Vitamin A, Vitamin K, Arsenic, Boron, Chromium, Copper, Iodine, Iron, Manganese, Molybdenum, Nickel, Silicon, Vanadium and Zinc*. 2000. The National Academy of Sciences Press, Washington DC. pp.1-773.
- 7114.** Jackson EK. Diuretics. Gilman AG, Hardman JG, Limbird LE, (eds.) In: *Goodman and Gilman's The Pharmacological Basis of Therapeutics*. 10th ed., New York, McGraw-Hill Companies. 2001:757-87.
- 7197.** Fawcett WJ, Haxby EJ, Male DA. Magnesium: physiology and pharmacology. *Br J Anaesth* 1999;83:302-20.
- 7207.** Crippa G, Sverzellati E, Giorgi-Pierfranceschi M, Carrara GC. Magnesium and cardiovascular drugs: interactions and therapeutic role. *Ann Ital Med Int* 1999;14(1):40-5.
- 7631.** Sigroth K. Letter: Effect of clonidine on nicotinic-acid flushing. *Lancet* 1974;2:58.
- 8552.** Adalat® CC (nifedipine extended-release tablets) package insert. West Haven, CT: Bayer Pharmaceuticals Corporation; 2008 May.
- 9771.** Pyridoxine hydrochloride injection, USP package insert. Schaumburg, IL: American Pharmaceutical Partners; 2005 Jun.