



Common Drug Classes, Drug-Nutrient Depletions, & Drug-Nutrient Interactions

Pharmavite LLC

Purpose: For educational use by health care professionals only.

Disclaimer: People taking prescription drugs may be more likely to have reduced levels of certain nutrients. Low nutrient levels may lead to other problems. Prescriptions are important to the consumer's health and will function without the recommended dietary supplements. The dietary supplements mentioned here are not intended to replace prescription drugs. It is important to advise consumers to consult with their health care provider before beginning a dietary supplement regimen.

DND = Drug Nutrient Depletion

General Recommendation for all Categories: Daily Multivitamin

DRUG CATEGORY	Drug Category Brief Description	Drug-Induced Nutrient Depletions	Additional Suggested Supplements for Nutritional Support*	Dietary Supplements that have Potential for Interactions with Drug (or Drug Class)**
<p>1. ACID-SUPPRESSING DRUGS and ANTACIDS</p> <p>Ex: Aciphex, Nexium, Prevacid, Prilosec, Protonix, Tagamet, Zantac, Pepcid and others</p>	<p>1. <u>H2 antagonists</u> block histamine (H2) receptors on gastric mucosal cells and decrease the production and secretion of acid</p> <p>2. <u>Proton-Pump Inhibitors</u> block the acid-transporter pump on the luminal surface preventing acid from entering the gastric lumen,</p> <p>3. <u>Antacids</u> directly neutralize existing acid in the stomach.</p>	<p>DND: H2 antagonists deplete calcium, iron, zinc, folic acid, vitamin D, and vitamin B12.</p> <p>Proton-pump inhibitors deplete vitamin B12 and magnesium.</p> <p>RECOMMENDED SUPPLEMENTATION:</p> <ul style="list-style-type: none"> H2 antagonists: <ul style="list-style-type: none"> * Calcium citrate: at least 500 mg per day (should be taken 1-2 hours after H2 antagonists) * Folic acid: 400 mcg/day H2 antagonists and proton-pump inhibitors: <ul style="list-style-type: none"> * Vitamin B12: 25-400 mcg/day * Magnesium: 250-400 mg/day 	<p>B-complex¹: 1/day</p> <p>Vitamin D²: 1000-2000 IU/day</p> <p>Zinc³: < 30 mg/day</p> <p>Iron⁴: discuss with health care provider.</p>	<p>Goldenseal and Ginger: These supplements may increase stomach acid and thus might interfere with antacids, H2 antagonists, and proton pump inhibitors.</p> <p>Green Tea: Tagamet (cimetidine) can inhibit the metabolism of caffeine in green tea and significantly reduce its clearance.</p>
<p>2. ANTIBIOTICS</p> <p>Ex: Amoxil, Augmentin, Bactrim, Ceclor, Cipro, Keflex, Levaquin, Avelox, Zithromax, and others</p>	<p>Antibiotics are used to treat bacterial infections.</p>	<p>DND: Antibiotics deplete folic acid, vitamin B1 (thiamin), vitamin B2 (riboflavin), vitamin B6, vitamin B12, calcium, magnesium, potassium, and vitamin K.</p> <p>RECOMMENDED SUPPLEMENTATION:</p> <ul style="list-style-type: none"> B-complex⁵: 1/day Calcium: 500-1000 mg/day in divided doses Magnesium: 250-400 mg/day 		<p>Calcium, Iron, Magnesium, and Zinc: When taken with antibiotics, these minerals can interfere with the absorption of the antibiotic (as well as the mineral) by forming insoluble complexes.</p> <p>Green Tea Catechins: Certain antibiotics (fluoroquinolones) reduce the clearance of some constituents of green tea (caffeine and theophylline) and may increase risk of their side effects: nervousness, palpitations and insomnia.</p> <p>St. John's Wort: St. John's Wort causes photosensitivity and may exacerbate the photosensitizing effects of certain antibiotics.</p>
<p>3. ANTICOAGULANTS/ ANTIPLATELETS <i>(continued page 2)</i></p> <p>Ex: Coumadin/Warfarin, Aspirin, Plavix, Ticlid, Aggrenox, and others</p>	<p>1. <u>Anticoagulants</u> decrease the potential for clotting via the Prothrombin-Thrombin-Fibrinogen cascade.</p> <p>2. <u>Antiplatelet drugs</u> decrease the potential for clots as a result of platelet aggregation.</p>			<p>The following supplements may enhance the effect of the medication and potentially increase risk of bleeding:</p> <p>Bilberry Cod Liver Oil Dong Quai Evening Primrose Oil</p>

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<p>3. ANTICOAGULANTS/ ANTIPLATELETS (continued from page 1)</p>				<p>Feverfew Fish Oil Flaxseed Oil Garlic Ginger Root Ginkgo Biloba Ginseng Glucosamine Goldenseal Grape Seed Extract Horse Chestnut Milk Thistle Saw Palmetto Vitamin E</p> <p>Vitamin K: People taking anticoagulant medications should maintain a consistent amount of vitamin K from their diet and supplement regimen, while avoiding fluctuations in intake or large doses of vitamin K.</p> <p>Coenzyme Q10: CoQ10 is structurally similar to vitamin K and may interfere with the drug's effectiveness.</p> <p>Goldenseal, Green Tea Catechins, Vitamin C: Concomitant use with warfarin may compromise therapeutic effects and alter International Normalized Ratio (INR) and/ or increase risk for clotting.</p>
<p>4. ANTIDEPRESSANTS Ex: Cymbalta, Effexor, Lexapro, Elavil, Paxil, Prozac, Norpramin, Remeron, Wellbutrin, Zoloft, Pristiq, Emsam and others</p>	<p>This class of medications increases the levels of one of more of the biogenic amines (e.g. norepinephrine, serotonin, dopamine) in the central nervous system. Clinical improvement from antidepressant therapy generally takes 3–6 weeks.</p>	<p>DND: SSRIs deplete folic acid.</p> <p>RECOMMENDED SUPPLEMENTATION:</p> <ul style="list-style-type: none"> • SSRIs: * Folic acid: 400 mcg/day 		<p>Melatonin: Melatonin may interact with medications that inhibit serotonin reuptake including a number of antidepressant medications (SSRIs, tricyclic antidepressants, venlafaxine, etc). Endogenous melatonin levels are reduced by SSRI medications.</p> <p>St. John's Wort and 5-HTP: St John's Wort and other supplements such as 5-HTP, in combination with other drugs that increase CNS serotonin levels (SSRIs, tricyclic antidepressants, venlafaxine, MAO inhibitors), can increase the risk of serotonergic side effects, including serotonin syndrome.</p> <p>SAM-e: Studies suggest SAM-e may augment the actions of antidepressant drugs in patients who are refractory to, or do not get full remission from their antidepressants.</p>

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<p>5. ANTIPILEPTIC DRUGS (ANTI-CONVULSANTS)</p> <p>Ex: Dylantin, Tegretol, Trileptal, Depakote, Topamax, Keppra, Neurontin, Lyrica and others</p>	<p>These drugs work by decreasing the firing of aberrant neurons in the brain and/or by decreasing the spread of abnormal activity to surrounding regions of the brain. There are various mechanisms of action of antiepileptic drugs.</p>		<p>Calcium⁶: 500 mg/day in divided doses Vitamin D⁷: 1000-2000 IU/day Vitamin B12⁸: 25–400 mcg/day</p>	<p>Use caution with the following supplements since they may interfere with the effectiveness of antiepileptic drugs.</p> <p>Folic Acid Ginkgo Biloba Niacin St. John's Wort</p>
<p>6. ANTI-HYPERTENSIVES: ACE Inhibitors, Angiotensin Receptor Blockers (ARBs), Calcium Channel Blockers, Beta Blockers, Diuretics</p> <p>Ex: Aldomet, Altace, Calan, Cardura, Cozaar, Hydrodiuril, Lotensin, Norvasc, Vasotec and others</p>	<p>The major classes of anti-hypertensive drugs are beta blockers, calcium channel blockers, ACE inhibitors, angiotensin receptor blockers, and thiazide diuretics. These drugs work to reduce blood pressure by decreasing total peripheral resistance or by reducing cardiac output, or both.</p>	<p>DND: ACE inhibitors deplete zinc.</p> <p>Calcium channel blockers and thiazide diuretics deplete potassium.</p> <p>Beta blockers deplete coenzyme Q10.</p> <p>RECOMMENDED SUPPLEMENTATION:</p> <ul style="list-style-type: none"> • ACE inhibitors: * Zinc: < 30 mg/day • Calcium channel blockers: * Potassium: < 100 mg/day • Thiazide diuretics: * Potassium: < 100 mg/day • Beta blockers * CoQ10: 100–200 mg/day 	<p>Iron⁹: Take as directed by health care provider</p>	<p>Potassium: (With ACE Inhibitors and ARBs only): Taking these drugs along with potassium supplements increases risk for hyperkalemia due to a decrease in renal potassium excretion.</p> <p>Calcium: (With calcium channel blockers only): Calcium supplements may interfere with the blood pressure lowering activity of these drugs.</p> <p>Vitamin D: (Verapamil only, a calcium channel blocker): Vitamin D supplements may interfere with the activity of verapamil.</p> <p>CoQ10 and Fish Oil: These supplements may decrease blood pressure in combination with anti-hypertensive drugs. Monitor blood pressure regularly.</p> <p>Green Tea Catechins and Goldenseal: These supplements may affect therapeutic benefits of anti-hypertensive drugs.</p> <p>Garlic, Ginkgo Biloba, St. John's Wort: These supplements have the potential to interfere with the cytochrome P450 system and therefore affect the metabolism and/or clearance of drugs. St. John's Wort also reduces the bioavailability of Verapamil.</p> <p>Calcium: Thiazide diuretics reduce calcium excretion by the kidneys and may increase risk for hypercalcemia, metabolic alkalosis, and possible renal failure.</p> <p>Melatonin: Melatonin may impair the efficacy of some calcium channel blockers (nifedipine). Monitor for changes in therapeutic efficacy of CCBs and adjust doses as necessary or avoid use of melatonin with this class of drugs.</p>

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<p>7. ANTIPSYCHOTICS</p> <p>Ex: Abilify, Seroquel, Zyprexa, Risperdal, Invega, Geodon, Haldol, Prolifen and others.</p>	<p>Antipsychotics block receptors for the neurotransmitters, dopamine, serotonin or both. They can reduce the symptoms of schizophrenia, decrease agitation and or aggression associated with other psychiatric conditions and may stabilize mood in bipolar disease.</p>	<p>DND: Vitamin B2 (riboflavin)</p> <p>RECOMMENDED SUPPLEMENTATION:</p> <ul style="list-style-type: none"> • Multivitamin: 1/day and/or • B-complex: 1/day 	<p>Vitamin C¹⁰: 250–500 mg/day</p>	<p>Echinacea: Echinacea may inhibit the human drug-metabolizing enzyme CYP1A2 leading to decreased clearance (increased blood levels) of Zyprexa or Clozaril and this increased potential for side effects.</p> <p>Evening Primrose Oil: Seizures have been reported in people with schizophrenia treated concomitantly with phenothiazine drugs (Chlorpromazine, Fluphenazine, Perphenazine, Promazine, and Thioridazine) and evening primrose oil.</p> <p>Goldenseal: Goldenseal can inhibit cytochrome P450 2D6 (CYP2D6) and might increase level and potential for side effects from a number of antipsychotic medications including Zyprexa, Risperdal, Abilify, Haldol and others.</p> <p>Ginseng: Ginseng may exacerbate some psychiatric conditions including hysteria, mania, and schizophrenia and thus compromise the therapeutic benefit of antipsychotics. Ginseng may also inhibit some of the drug metabolizing enzymes responsible for clearance of a number of antipsychotic drugs.</p> <p>Ginkgo Biloba: Ginkgo has been reported to cause seizures or lower seizure threshold. Thus, in combination with drugs that lower seizure threshold (including antipsychotics) the combination might significantly increase risk of seizures.</p> <p>St. John's Wort: St John's Wort in combination with other psychotropic drugs, including antipsychotics, may lead to unpredictable effects. St. John's Wort is known to cause photosensitivity therefore using it with other photosensitizing drugs such as phenothiazine antipsychotic drugs may increase the risk of photosensitivity.</p>
<p>8. BENZODIAPEZINES:</p> <p>Ex: Diazepam, Clorazepate, lorazepam, klonopin, alprazolam and others.</p>	<p>Benzodiazepines are a class of drugs primarily used to treat anxiety.</p>	<p>DND: Melatonin Endogenous melatonin is depleted by benzodiazepines.</p> <p>Calcium These medications decrease calcium absorption by increasing metabolism of vitamin D, which is needed for calcium absorption.</p> <p>RECOMMENDED SUPPLEMENTATION:</p> <ul style="list-style-type: none"> • Calcium: 500–1000 mg/day taken in divided dose 		<p>Kava: The combination of kava and benzodiazepines is not recommended due to their similar effects.</p>

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<p>9. CHOLESTEROL-LOWERING DRUGS: STATINS</p> <p>Ex: Lipitor, Crestor, Pravachol, Zocor, Lescol, Mevacor, and others</p>	<p>Statins inhibit the enzyme HMG CoA reductase—a key step in the hepatic synthesis of cholesterol. The reduction of cholesterol synthesis subsequently increases the liver's removal of circulating LDL cholesterol.</p> <p>Note: HMG CoA reductase is also a key enzyme in the synthesis of Coenzyme Q10.</p>	<p>DND: CoQ10</p> <p>Statins inhibit the enzyme HMG CoA reductase.</p> <p>RECOMMENDED SUPPLEMENTATION: CoQ10: 100–200 mg/day</p>	<p>Fish oil¹¹: 500–1000 mg EPA+DHA/day</p>	<p>St. John's Wort and Garlic (containing allicin): St. John's Wort may increase the metabolism (cytochrome P450 ~ CYP3A4) of some of the statins leading to decrease serum concentrations of these drugs and possibly diminished effectiveness.</p> <p>Vitamin A: Long term use of cholesterol-lowering drugs may increase vitamin A levels in the blood. Vitamin A levels may need to be monitored in some people.</p> <p>Red Yeast Rice: Red yeast rice contains lovastatin which also lowers blood cholesterol levels. This supplement should not be taken with cholesterol lowering drugs unless under the supervision of a healthcare professional.</p>
<p>10. DIGOXIN</p> <p>Ex: Digitek, Lanoxicaps, Lanoxin, Cardoxin</p>	<p>Digoxin is derived from the leaves of the <i>Digitalis lantata</i> plant (a variety of foxglove). It is used to treat heart failure and atrial fibrillation.</p>	<p>DND: Calcium, magnesium, phosphorus, vitamin B1 (thiamin), and potassium</p> <p>RECOMMENDED SUPPLEMENTATION:</p> <ul style="list-style-type: none"> • Calcium: 500–1000 mg/day in divided doses • Magnesium¹²: 250–400 mg/day • B-complex: 1/day • Potassium: < 100 mg/day 		<p>Calcium: High levels of calcium increase the likelihood of a toxic reaction to digoxin. Low levels of calcium interfere with the function of digoxin. Consistent intake of calcium and monitoring of calcium levels by a healthcare professional is recommended.</p> <p>Hawthorn: The activity of digoxin may be enhanced by hawthorn supplements.</p> <p>St. John's Wort: St. John's Wort supplements may reduce serum levels of digoxin.</p>
<p>11. DIURETICS</p> <p>Ex: Lasix, Microzide (HCTZ), Zaroxolyn, Aldactone, Diamox and others</p>		<p>DND: Loop and Thiazide Diuretics deplete magnesium, potassium, and zinc.</p> <p>Potassium sparing diuretics deplete folic acid.</p> <p>RECOMMENDED SUPPLEMENTATION:</p> <ul style="list-style-type: none"> • Loop and Thiazide Diuretics: <ul style="list-style-type: none"> * Magnesium: 250 mg/day * Potassium: < 100 mg/day * Zinc: < 30 mg/day • Potassium-sparing diuretics: <ul style="list-style-type: none"> * Folic acid: 400 mcg/day 		<p>CoQ10 and Fish Oil: When taken together with diuretics these supplements may have additive blood pressure lowering effects and increase risk for hypotension.</p> <p>Ginkgo Biloba: Ginkgo may reduce the effectiveness of some diuretics.</p>

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<p>12. HORMONE REPLACEMENT THERAPY (ESTROGENS)</p> <p>Ex: Estrace, Premarin and Prempro</p>	<p>Hormone replacement therapy is used to replace female hormones that are no longer produced after menopause.</p>	<p>DND: Vitamin B6 Folic acid Magnesium</p> <p>RECOMMENDED SUPPLEMENTATION:</p> <ul style="list-style-type: none"> • Vitamin B6: 5 mg/day • Folic acid: 400 mcg/day • Magnesium: 250–400 mg/day 	<p>B-complex¹³: 1/day</p>	<p>Calcium and Vitamin D: Calcium and Vitamin D may increase absorption of hormone replacements. These supplements are recommended to improve bone mineral density during estrogen therapy.</p> <p>Zinc and Magnesium: Excretion of these minerals is reduced by hormone replacement therapy.</p> <p>Red Clover Extract and Soy Isoflavones: These supplements may interfere with the activity or absorption of hormone replacement therapy.</p> <p>St. John's Wort: St. John's Wort may alter hormone metabolism including estrogen and progesterone. This supplement is not recommended during hormone replacement therapy.</p> <p>Caffeine: The stimulating effects of caffeine may be increased due to inhibition of metabolism or clearance of caffeine by hormone replacement therapy.</p>
<p>13. ORAL CONTRACEPTIVES</p> <p>Ex: Alesse, Demulen, Ortho-cyclen, Seasonale, TriPhasil, Yasmin and others</p>	<p>Synthetic and semi-synthetic analogs of estrogen and/or progesterone used to prevent pregnancy by (1) inhibiting ovulation and/or (2) thickening cervical mucus (3) diminishing endometrial integrity</p>	<p>DND: Vitamin B6 Folic acid Magnesium</p> <p>RECOMMENDED SUPPLEMENTATION:</p> <ul style="list-style-type: none"> • Vitamin B6: 5 mg/day • Folic acid: 400 mcg/day • Magnesium: 250–400 mg/day 	<p>Calcium¹⁴: 500 mg/day</p> <p>Folic acid¹⁵: 400 mcg/day</p> <p>B-complex¹⁶: 1/day</p>	<p>St. John's Wort and Garlic: St. John's Wort and garlic supplements may decrease the effectiveness of oral contraceptives. Women taking St. John's Wort and/or garlic supplements along with oral contraceptives should use an additional form of birth control. St. John's Wort also causes photosensitivity which may be exacerbated by oral contraceptives.</p> <p>Green Tea Catechins: Use caution with green tea and oral contraceptives. Oral contraceptives can decrease caffeine clearance by 40–65% and may increase adverse effects of caffeine in green tea. Adjust dose or discontinue if necessary.</p> <p>Iron and Copper: Oral contraceptives may increase serum iron and copper levels.</p>

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<p>14. ORAL HYOGLYCEMICS</p> <p>Ex: Actos, Amaryl, Avandia, Diabeta, Glucophage, Glucotrol, Glucovance, Metaglip, Prandin, Januvia, Byetta and many others</p>	<p>There are 5 subclasses of oral hypoglycemics that work by either:</p> <ul style="list-style-type: none"> Stimulating the secretion of insulin from the pancreas (sulfonylureas, meglitinides) Improving insulin sensitivity (thiazolidinediones) Decreasing production of glucose in the liver (biguanides) Reducing the absorption of dietary glucose (alpha-glucosidase inhibitors). 	<p>DND: Vitamin B12 Folic acid</p> <p>RECOMMENDED SUPPLEMENTATION:</p> <ul style="list-style-type: none"> Vitamin B12: 25–400 mcg/day Folic acid: 400 mcg/day 	<p>B-complex¹⁷: 1/day CoQ10¹⁸ : 100–200 mg/day</p>	<p>The following supplements may interfere with the effectiveness of the drug, or cause additive blood glucose-lowering effects and increase the risk of hypoglycemia when used in combination with certain antidiabetic drugs.</p> <p>Alpha Lipoic Acid Bilberry Chromium Garlic Ginkgo Biloba Ginseng Green Tea Catechins Melatonin St. John's Wort</p>

*Suggested supplements that may support overall health and are not at all intended to replace any prescription medications.

**These supplements listed may have the potential to interact with the drug or drug class. Use caution or avoid these supplements unless approved by your physician or preferred health care provider.

- ¹ Vitamin B12, folic acid and vitamin B6 help maintain healthy homocysteine levels. Increased homocysteine levels in the blood may negatively impact vascular health.
- ² Vitamin D is essential for optimal absorption of calcium.
- ³ H2 antagonists deplete zinc, however, zinc supplementation may not be recommended for all individuals. Consult your health care provider regarding proper supplementation along with current health status, health history and individual medication use.
- ⁴ Iron is depleted by H2 antagonists, however, iron should not be routinely supplemented while taking H2 antagonists. High levels of iron cause unnecessary oxidative stress and other undesirable symptoms. Iron supplementation is only recommended for those who suffer symptoms of iron depletion (e.g. anemia).
- ⁵ The destruction of normal gastrointestinal flora by antibiotics can cause a decrease in the normal bacterial production of certain B vitamins.
- ⁶ Dylantin, Phenobarbital and Tegretol can increase the metabolism/clearance of vitamin D, leading to a subsequent decrease in calcium absorption. Hypocalcemia and osteomalacia have been reported, particularly in cases of prolonged therapy with combinations.
- ⁷ These medications decrease calcium absorption by increasing metabolism of vitamin D (which is needed for calcium absorption). Individuals taking these supplements for 6 months or more should consider calcium and vitamin D supplements.

- ⁸ Dylantin, Phenobarbital and Mysoline have been reported to reduce vitamin B12 absorption as well as serum and cerebrospinal fluid vitamin B12 levels in some patients. Megaloblastic anemia and neuropsychiatric side effects have been associated with these drugs.
- ⁹ Low-dose ferrous sulfate supplements may help to alleviate ACE inhibitor-related cough.
- ¹⁰ Vitamin C taken in adjunct with atypical antipsychotics may reduce oxidative stress.
- ¹¹ Omega-3 fatty acids EPA and DHA support heart health.
- ¹² Digoxin decreases renal tubular reabsorption of magnesium, thereby increasing magnesium excretion in the urine. Individuals taking digoxin for heart failure may also be taking loop or thiazide diuretics, which may potentially increase risk for hypomagnesemia.
- ¹³ A daily B complex supplement provides vitamin B6 as well as other key B vitamins, all of which work together in the body.
- ¹⁴ Calcium supplementation may be warranted with oral contraceptive use to help maintain bone health if dietary calcium intake is inadequate.
- ¹⁵ All women of childbearing age should supplement with 400 mcg/day of folic acid to support a healthy pregnancy.
- ¹⁶ Certain oral contraceptives, particularly higher dose forms, can lower serum levels of vitamin B1 (thiamin), vitamin B2 (riboflavin), niacin, and vitamin B12.
- ¹⁷ The drug glucophage (metformin) may reduce the absorption of vitamin B12 in the body.
- ¹⁸ CoQ10 provides antioxidant support against oxidative stress, supports cellular energy production, and helps support heart function.

References are available upon request.



ABOUT PHARMAVITE LLC

For over 40 years, Pharmavite LLC has earned and maintained the trust of healthcare professionals, consumers and retailers by manufacturing high-quality vitamins, minerals, other dietary supplements and all-natural foods under its Nature Made® and SOYJOY® brand names.

Nature Made® is the #1 national vitamin and supplement brand in the food, drug, club and mass channels.* As the industry leader in standards for dietary supplements, Nature Made® became the first national vitamin brand in the U.S. to earn United States Pharmacopeia (USP) verification on many of its products. USP is a scientific, nonprofit organization that has been setting federally-recognized, public standards of quality for medicines, dietary supplements and food ingredients.

Additionally, Pharmavite's commitment to Good Manufacturing Practices (GMPs) and quality extends to every aspect of our production, from purchasing high-quality raw materials, to the meticulous production and testing of every product. The dietary supplement industry is regulated by the U.S. Food and Drug Administration and the Federal Trade Commission, as well as by government agencies in each of the 50 states.

Pharmavite's emphasis on health and nutrition knowledge, emerging scientific research and new technology has enabled us to forge compelling partnerships with many distinguished educational institutions. The end result is that Pharmavite stays on the leading edge of key scientific advancements and innovations that make a difference in people's lives. Based in Northridge, California, Pharmavite LLC operates as a subsidiary of Otsuka Pharmaceutical Co., Ltd. For more information, please visit <http://www.pharmavite.com>.

* Pharmavite calculation based in part on data reported by Nielsen through its Scantrack® service for the Dietary Supplements category in dollar and unit sales for the 52-week period ending 12/22/2012 in US xAOC channels. ©2013 The Nielsen Company