

# Nutritional Supplement Formulary

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Houston EMA Ryan White Part A

**Ryan White Grant Administration**

**March 2014**

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## Overview

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In the 1st quarter of 2012, Ryan White Grant Administration (RWGA) surveyed Ryan White funded medical care clinicians on their views regarding nutritional supplements\therapy. Findings from that survey indicated that clinicians favored greater limitations on the types of supplements available to patients. Based on this feedback, and with the support of the Ryan White Planning Council's Quality Assurance Committee, RWGA began the development of a formulary for the nutritional supplement service category.

RWGA began development of the formulary by further surveying funded clinicians and consumers to determine perceived nutritional supplement usage. RWGA also reviewed the nutritional supplement service category billing history for additional usage information.

To gather information on evidence based clinical benefits of nutritional supplements, RWGA utilized Natural Standard database ([www.naturalstandard.com](http://www.naturalstandard.com)). Natural Standard database is a collection of systematic reviews of alternative and complementary medicine is primarily geared toward clinicians who intend to provide information to help make informed therapeutic decisions<sup>1</sup>. Natural Standard employs a grading system to rate the value of supplement to improve a given condition based on scientific evidence.

In 3<sup>rd</sup> quarter 2012 all development activities findings were presented to the Ryan White Clinical Quality Management Committee (Committee) for review. The Committee agreed to a formulary consisting of evidence based supplements identified by local provider and consumer surveys as most appropriate and/or more often used (see list below).

- Calcium
- Fiber
- Fish oil
- Folate
- Iron
- Magnesium
- Meal Replacement (e.g. Ensure, Glucerna, etc.)
- Multi-vitamins
- Protein Powder (Whey)
- Vitamin B
- Vitamin C
- Selenium

Clinical providers wishing to prescribe/order other supplements not on the formulary will submit a formulary addition form to RWGA prior to doing so (see attachment 1). All completed requests submitted by applicable agency clinician (MD, DO, NP, PE, Pharmacist) will be submitted to the Clinical Quality Management Committee for review and approval annually.

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<sup>1</sup> N Mani, Natural Standard, Journal of the Medical Library Association. 2005 Oct; 93(4)507-509

## Formulary Grading System

### Natural Standard evidence-based validated grading rationale <sup>TM</sup>

- Grades reflect the level of available scientific evidence in support of the efficacy of a given therapy for a specific indication.
- Expert opinion and folkloric precedent are not included in this assessment, and are reflected in a separate section of each monograph ("Strength of Expert Opinion and Historic / Folkloric Precedent")
- Evidence of harm is considered separately; the below grades apply only to evidence of benefit.

Level of Evidence Grade	Criteria
A (Strong Scientific Evidence)	Statistically significant evidence of benefit from >2 properly randomized trials (RCTs), OR evidence from one properly conducted RCT AND one properly conducted meta-analysis, OR evidence from multiple RCTs with a clear majority of the properly conducted trials showing statistically significant evidence of benefit AND with supporting evidence in basic science, animal studies, or theory.
B (Good Scientific Evidence)	Statistically significant evidence of benefit from 1-2 properly randomized trials, OR evidence of benefit from >1 properly conducted meta-analysis OR evidence of benefit from >1 cohort/case-control/non-randomized trials AND with supporting evidence in basic science, animal studies, or theory. This grade applies to situations in which a well-designed randomized controlled trial reports negative results but stands in contrast to the positive efficacy results of multiple other less well designed trials or a well-designed meta-analysis, while awaiting confirmatory evidence from an additional well designed randomized controlled trial.
C (Unclear or Conflicting Scientific Evidence)	Evidence of benefit from >1 small RCT(s) without adequate size, power, statistical significance, or quality of design by objective criteria,* OR conflicting evidence from multiple RCTs without a clear majority of the properly conducted trials showing evidence of benefit or ineffectiveness, OR evidence of benefit from >1 cohort/case-control/non-randomized trials AND without supporting evidence in basic science, animal studies, or theory, OR evidence of efficacy only from basic science, animal studies, or theory.

D (Fair Negative Scientific Evidence)	Statistically significant negative evidence (i.e., lack of evidence of benefit) from cohort/case-control/non-randomized trials, AND evidence in basic science, animal studies, or theory suggesting a lack of benefit. This grade also applies to situations in which >1 well designed randomized controlled trial reports negative results, notwithstanding the existence of positive efficacy results reported from other less well designed trials or a meta-analysis. (Note: if there is >1 negative randomized controlled trials that are well designed and highly compelling, this will result in a grade of "F" notwithstanding positive results from other less well designed studies.)
F (Strong Negative Scientific Evidence)	Statistically significant negative evidence (i.e., lack of evidence of benefit) from >1 properly randomized adequately powered trial(s) of high-quality design by objective criteria.*
Lack of Evidence	Unable to evaluate efficacy due to lack of adequate available human data.

\* Objective criteria are derived from validated instruments for evaluating study quality, including the 5-point scale developed by Jadad et al., in which a score below 4 is considered to indicate lesser quality methodologically (Jadad AR, Moore RA, Carroll D, Jenkinson C, Reynolds DJ, Gavaghan DJ, McQuay HJ. Assessing the quality of reports of randomized clinical trials: is blinding necessary? *Controlled Clinical Trials* 1996; 17[1]:1-12).

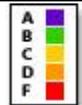
## Acidophilus

Natural Standard Professional Monograph, Copyright © 2013 (www.naturalstandard.com).

### Synonyms/Common Names/Related Substances:

Acidophilus, Acidophilus Extra Strength®, acidophilus milk, Acilact, Actimel® Cholesterol Control, Bio-K+®, Calagin®, DDS-Acidophilus, Enpac®, Florajen®, fresh poi, Kyo-Dophilus®, L-92, L. amylovorus, L. gallinarum sp. nov. (ATCC 33199), L. johnsonii sp. nov. (ATCC 33200), Lacteol Fort®, lactic acid bacteria mixture (Oxadrop® or AKSB), lactic acid-producing bacteria (LAB), Lacto Bacillus, Lactobacillaceae (family), lactobacilli, lactobacilo acidofilo, lactobacillus, Lactobacillus acidophilus, Lactobacillus acidophilus 74-2, Lactobacillus acidophilus 145, Lactobacillus acidophilus ATCC 4356, Lactobacillus acidophilus B, Lactobacillus acidophilus BG2F04, Lactobacillus acidophilus CL1285, Lactobacillus acidophilus CUL60, Lactobacillus acidophilus DDS-1, Lactobacillus acidophilus E, Lactobacillus acidophilus group A3, Lactobacillus acidophilus L-92, Lactobacillus acidophilus LA 02, Lactobacillus acidophilus La5, Lactobacillus acidophilus milk, Lactobacillus acidophilus N1, Lactobacillus acidophilus NCFM, Lactobacillus acidophilus NCK56, Lactobacillus acidophilus OLL2769, Lactobacillus acidophilus Rosell-52, Lactobacillus acidophilus spp., Lactobacillus acidophilus strain 27L, Lactobacillus acidophilus strain LB (LaLB), Lactobacillus acidophilus-SDC 2012, Lactobacillus acidophilus-SDC 2013, Lactobacillus acidophilus yogurt, Lactobacillus amylovorus, Lactobacillus gallinarum sp. nov. (ATCC 33199), Lactobacillus johnsonii sp. nov. (ATCC 33200), Lactobacillus LB, Narine®, poi, Probiata®, probiotic, sour poi, Vitaflor, Vivag®, yogurt.

### Scientific Evidence for Common/Studied Uses:

Indication	Evidence Grade	 Grading System
Vaginal disorders	B	
Diarrhea prevention	C	
Immune function	C	

### Brief Safety Summary:

- Likely safe:** Oral L. acidophilus is likely safe in the general population of children and adults, when consumed appropriately. L. acidophilus is likely safe as a suppository for women.
- Possibly safe:** When used orally and appropriately in pregnancy (2-4 weeks before delivery) and lactation (for up to six months). When used orally and appropriately in the elderly.
- Possibly unsafe:** When used in individuals with short bowel syndrome, as bacteremia has been reported after ingestion of Lactobacillus. When used in individuals with high fever, according to secondary sources. When used in infants and children, although L. acidophilus colonization is associated with a decreased incidence of colic in infants, and there is a lack of evidence regarding the safety of long-term use of L. acidophilus or other probiotics in infants. There have been reports of pediatric probiotic use with subsequent bacteremia and sepsis involving probiotic strains of Lactobacilli and a report of severe dehydration in a child with diarrhea following treatment with oral rehydrating solution and Lacteol®. When used in patients with gastrointestinal (GI) disorders, as high doses (over 109 cells daily) have been associated with mild GI disturbances. When used in individuals with fixed orthodontic appliances, occlusal disturbances, or malocclusion, as this microorganism may be cariogenic.
- Likely unsafe:** When used in individuals who are immunodeficient, as Lactobacillus may cause pathogenic colonization, particularly in those who are immunocompromised. When used in individuals who have milk allergies, due to possible milk allergens being present in L. acidophilus

preparations derived from dairy products, according to secondary sources. When used in individuals with known allergy or hypersensitivity to *Lactobacillus acidophilus*, its constituents, or members of the Lactobacillaceae family.

## Calcium

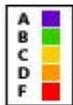
Natural Standard Professional Monograph, Copyright © 2013 (www.naturalstandard.com).

### Synonyms/Common Names/Related Substances:

Acétate de calcium (French), AdvaCAL<sup>®</sup>, Alka-Mints<sup>®</sup>, Apo-Cal<sup>®</sup>, aspartate de calcium (French), atomic number 20, Bica<sup>®</sup>, bone meal, Bo-Ne-Ca<sup>®</sup>, bovine cartilage, Ca, Ca++, Ca2+, Cal-100<sup>®</sup>, Calcanate<sup>®</sup>, Calcefor<sup>®</sup>, Calci Aid<sup>®</sup>, Calci-Fresh<sup>®</sup>, Calcigamma<sup>®</sup>, Calcilos<sup>®</sup>, Calcimax<sup>®</sup>, Calcit<sup>®</sup>, calcitonin, Calcitridin<sup>®</sup>, calcitriol, calcium acetate, calcium aspartate, calcium carbonate, calcium chelate, calcium chloride, calcium citrate, calcium citrate malate, Calcium Dago<sup>®</sup> (Germany), calcium formate, calcium gluceptate, calcium gluconate, calcium hydroxide, Calcium Klopfer<sup>®</sup> (Austria), calcium lactate, calcium lactate gluconate, calcium lactogluconate, calcium orotate, calcium oxalate, calcium oxide, Calcium Pharmavit<sup>®</sup> (Hungary), calcium phosphate, calcium pyruvate, Calcium-Sandoz Forte<sup>®</sup> (Bulgaria), Calcuren<sup>®</sup> (Finland), Caldoral<sup>®</sup> (Colombia), Calmate<sup>®</sup> 500 (Philippines), CalMax<sup>®</sup>, Calmicid<sup>®</sup>, Cal-Quick<sup>®</sup>, Calsan<sup>®</sup> (Mexico, Peru, Philippines), Calsup<sup>®</sup>, Cal-Sup<sup>®</sup> (New Zealand), Caltab<sup>®</sup> (Thailand), Caltrate<sup>®</sup> (Puerto Rico, Colombia, Malaysia, Mexico, South Africa), Caltrate 600<sup>®</sup> (Canada, Colombia, Costa Rica, Dominican Republic, Ecuador, El Salvador, Guatemala, Honduras, Nicaragua, Panama, Peru, Venezuela), Cantacid<sup>®</sup> (Korea), Cartilade<sup>®</sup>, CC-Nefro 500<sup>®</sup> (Germany), chelated calcium, Chooz<sup>®</sup>, Chooz Antacid Gum 500<sup>®</sup> (Israel), Citrical<sup>®</sup>, clacked lime, coral calcium, dairy products (milk, cheese, yogurt, etc.), dialysate calcium, dicalcium phosphate, Dimacid<sup>®</sup>, dolomite, Estroven<sup>®</sup>, Fixical<sup>®</sup> (France), Gaviscon<sup>®</sup>, heated oyster shell-seaweed calcium, hydroxyapatite, isotopically enriched milk (oral 44Ca and intravenous 42Ca), LeanBalance<sup>®</sup>, lime, Living Calcium<sup>®</sup>, Maalox<sup>®</sup>, Maalox<sup>®</sup> Quick Dissolve (Canada), magnesium, Netra<sup>®</sup> (Israel), Neutralin<sup>®</sup>, Noacid<sup>®</sup> (Uruguay), nonfat milk, Orocal<sup>®</sup> (France), Os-Cal<sup>®</sup>, Ospur<sup>®</sup> Ca 500 (Germany), Osteo Wisdom<sup>®</sup>, Osteocal<sup>®</sup> 500 (France), osteocalcin, Osteomin<sup>®</sup> (Mexico), OsteoPrime<sup>®</sup>, oyster shell calcium, oyster shell electrolytate (OSE), Pepcid<sup>®</sup> Complete, Pluscal<sup>®</sup> (Argentina), Posture-D<sup>®</sup>, Renacal (Germany), Rocaltrol<sup>®</sup>, Roloids<sup>®</sup>, salmon calcitonin, Sandocal<sup>®</sup>, shark cartilage, tricalcium phosphate, Tums<sup>®</sup>, Tums Ultra Assorted Berries<sup>®</sup> (Israel), Tums Ultra Spearmint<sup>®</sup> (Israel), Tzarevet X<sup>®</sup> (Israel), Viactiv<sup>®</sup>.

### Scientific Evidence for Common/Studied Uses:

Indication	Evidence Grade
Antacid	A
Bone density	A
High blood phosphorous level	A
Hypocalcemia	A
Hypocalcemic tetany	A
Osteoporosis	A
Renal failure	A
Toxicity (magnesium)	A
Black widow spider bite	B
Fractures (prevention)	B
Gastrointestinal tract and colorectal cancer prevention	B
High blood potassium level	B
Hypertension	B
Lead toxicity	B



Grading System

Pre-eclampsia	B	
Premenstrual syndrome (PMS)	B	
Seizures	B	

**Brief Safety Summary:**

- Likely safe:** According to secondary sources, calcium supplementation is likely safe when used orally and intravenously, as suggested by a qualified healthcare professional. It is also likely safe when used orally and appropriately in pregnancy and lactation, as recommended by a qualified healthcare professional. Routine dietary intake and supplementation in recommended doses are not associated with significant adverse effects.
- Possibly unsafe:** According to secondary sources, calcium is possibly unsafe when used in excess: the daily tolerable upper intake level (UL) of elemental calcium by age is as follows: 0-6 months, 1,000mg; 6-12 months, 1,500mg; 1-3 years, 2,500mg; 9-18 years, 3,000mg; 19-50 years, 2,500mg; 51+ years, 2,000mg. When used with aluminum- and magnesium-containing antacids; antiarrhythmics ; anticoagulants; anticonvulsants; antidiabetics; antihypertensives; antilipemics, although conflicting evidence exists; bisphosphonates; calcium channel blockers, according to secondary sources, although conflicting evidence exists; diuretics; calcipotriene (Dovonex®); tetracycline, fluoroquinolones, and gentamicin, all according to secondary sources; quinolones; gadoversetamide; H2 antagonists; inositol hexaphosphate (phytic acid); iron salts, although conflicting evidence exists; lithium; Orlistat (Xenical®), according to secondary sources; oxalic acid, according to secondary sources; parathyroid agents (cinacalcet); hypothyroidism or taking thyroxine, according to secondary sources; magnesium; potassium; sodium alginate, according to secondary sources; steroids; large amounts of vitamin D, according to secondary sources; or zinc, according to secondary sources. When used in those with achlorhydria (calcium carbonate and tribasic calcium phosphate tablets, according to secondary sources); in individuals with heart arrhythmias and ventricular fibrillation, according to secondary sources; in patients with hyperphosphatemia or hypophosphatemia, according to secondary sources; in postmenopausal women due to an increased possibility of cardiovascular side effects; and in those prone to the formation of calcium-containing kidney stones.
- Likely unsafe:** When used in patients using sodium polystyrene sulfonate, according to secondary sources; in those with digoxin (i.e., digitalis) toxicity or those using digoxin, although conflicting evidence exists; in those with hypercalcemia, hypercalciuria, hyperparathyroidism, bone tumors, or sarcoidosis, according to secondary sources; in chronic renal failure patients, especially in those taking aluminum-containing agents; and in patients (two months old or younger) using ceftriaxone. When calcium supplements made from dolomite, oyster shells, or bone meal are used, due to possible lead toxicity, according to secondary sources. When used by chronic renal failure patients taking aluminum-containing agents, as in humans, calcium citrate increased intestinal aluminum absorption. Citrate-containing preparations are contraindicated in chronic renal failure patients taking aluminum-containing compounds.
- Note:** Excretion of abnormally large amounts of calcium in the urine is a well-established side effect of administration. Avoid cigarette smoking, as it decreases intestinal calcium absorption and may lead to decreased bone mineral density, according to secondary sources. In patients with achlorhydria, calcium carbonate and tribasic calcium phosphate tablets are not suggested.

## Folate

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### Synonyms/Common Names/Related Substances:

5-Methyltetrahydrofolate, B complex vitamin, Equaline™, folacin, folic acid, folinic acid, Folvite®, heptaglutamyl folic acid, hexaglutamyl folic acid, L-5-methyltetrahydrofolate, leucovorin, methyltetrahydrofolate, monoglutamyl folic acid, Nature Made®, Nutri Plus®, polyglutamyl folic acid, pteroylglutamic acid, pteroylmonoglutamic acid, pteroylpolyglutamate, Safeway™, Sunmark™, vitamin B9, vitamin M, Your Life®.

**Select combination products:** Beyaz™ (birth control pill plus folate).

### Scientific evidence for common/studied uses:

Indication	Evidence Grade	 Grading System
Folate deficiency	A	
Folate deficiency in alcoholics	A	
Hyperhomocysteinemia	A	
Megaloblastic anemia - due to folate deficiency	A	
Prevention of pregnancy complications/ neural tube defects	A	
Methotrexate toxicity	B	

### Brief Safety Summary:

- Likely safe:** When used as an additive, folic acid may be added to foods; breakfast cereals: at levels below 400mcg per serving; infant formula: 4mcg per 100 kcal of infant formula; corn grits: 1mg per lb.; meal-replacement products: 200mcg or 400mcg per serving, depending on whether the food is represented for use once or more than once daily. In medical foods, it may be added at levels not to exceed the amount necessary to meet the distinctive nutritional requirements of the disease or condition for which the food is formulated. For foods for special dietary use, levels are not to exceed the amount necessary to meet the special dietary needs for which the food is formulated.

The dietary reference intake levels in the United States and Canada are as follows: males over 13 years, 400mcg; females over 13 years, 400-600mcg; pregnancy all ages, 400-600mcg; nursing (lactation) all ages, 500mcg. In children, the suggested intake levels are as follows: babies 0-6 months, 65mcg; 7 to 12 months, 80mcg; children 1-3 years, 150mcg; children 4-8 years, 200mcg; males 9-13 years, 300mcg; males over 13 years, 400mcg; females 9-13 years, 300mcg; females over 13 years, 400-600mcg; pregnancy all ages, 400-600mcg; nursing (lactation) all ages, 500mcg.

Tolerable upper intake levels (UL) daily: 1-3 years of age, 300mcg daily; 4-8 years, 400mcg; 9-13 years, 600mcg; 14-18 years, 800mcg; 14-18 years of age (including pregnant or breastfeeding women), 800mcg; and 19 years and older (including pregnant or breastfeeding women), 1,000mcg.

- Possibly unsafe:** When used as supplemental doses above the tolerable UL, without direction of a medical professional. When used in individuals living in a high malaria area; in patients at risk

of cancer) folic acid injections containing benzyl alcohol (1.5%) as a preservative should be used only under the advice of a healthcare provider; in patients with low blood pressure or in those using hypotensives; in patients with skin concerns (secondary sources); in combination with aspirin; in patients with gastrointestinal concerns (secondary sources); in individuals at risk of anemia; in patients with neurological disorders (secondary sources); in patients with seizure disorders (secondary sources); in patients with respiratory disorders; in individuals with low blood sugar or in those using hypoglycemics.

- **Likely unsafe:** When used with a combination of B vitamins in patients following coronary stenting (secondary sources) or in patients prescribed anticancer agents or folic acid antagonists (secondary sources), unless prescribed by a healthcare professional.

**Note:** The "safe level of intake" of 1mg folate daily set by the U.S. FDA may cause a serum folic acid effect. The folic acid effect is the presence of unmetabolized folic acid in the blood.

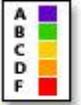
## Iron (Fe)

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### Synonyms/Common Names/Related Substances:

Atomic number 26, carbonyl iron, dextran-iron, elemental iron, FE, Fer, ferric ammonium chloride, ferric chloride, ferric citrate, ferric phosphate, ferric pyrophosphate, ferric sodium pyrophosphate, ferric sulfate, ferrous ascorbate, ferrous carbonate, ferrous carbonate anhydrous, ferrous citrate, ferrous fumarate, ferrous fumarate sprinkles, ferrous gluconate, ferrous lactate, ferrous pyrophosphate, ferrous sulfate, heme-iron, iron dextran, iron proteinsuccinylate, iron sorbitol, iron sucrose, iron sulfate, iron(III)-hydroxide polymaltose complex, iron-choline citrate complex, iron-polysaccharide, iron-polysterene sulphonate, ITF 282, NaFeEDTA, nonheme iron, reduced iron, saccharated iron, sodium ferric gluconate, sodium ferric gluconate complex (SFGC), sodium iron ethylenediaminetetra-acetate.

### Scientific evidence for common/studied uses:

Indication	Evidence Grade	 Grading System
Anemia of chronic disease	A	
Iron deficiency anemia	A	
ACE inhibitor-associated cough	B	
Preventing iron deficiency in menstruating women	B	
Prevention of iron deficiency anemia in pregnancy	B	

### Brief Safety Summary:

- **Likely safe:** When used orally in doses not exceeding the recommended dietary allowance (RDA).
- **Possibly safe:** When used in pregnant women, as iron is recognized as a Pregnancy Category B drug by the FDA.
- **Possibly unsafe:** When used in pregnant women for replenishing depleted iron stores in the bone marrow, where it is incorporated into hemoglobin, as iron use is recognized by the FDA as a Pregnancy Category C drug for this particular use in pregnancy. When used in uremic patients treated with periodic dialysis, as hypersiderosis (uncontrollable sweating) has been reported with long-term iron supplementation in such patients. When used in patients with gastrointestinal disorders, as nausea, vomiting, heartburn, epigastric or abdominal pain, constipation, and diarrhea have been reported. A case of ferrous sulfate-induced gastric mucosal injury following long-term use has also been reported. When iron preparations are used, as they may possibly blacken or stain teeth. When used in people with a history of kidney disease, intestinal disease, enteritis, colitis, pancreatitis, or hepatitis, or those who consume excessive alcohol, plan to become pregnant, or are over age 55 and have a family history of heart disease. Secondary sources suggest that these patient populations should consult a healthcare provider before taking iron.
- **Likely unsafe:** When used in patients with or at risk for iron overload due to hemochromatosis or any other cause. When used in individuals sensitive or allergic to iron products. When used in patients with hemolytic anemia, according to secondary sources.

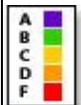
## Magnesium

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### Synonyms/Common Names/Related Substances:

Chelated magnesium, Emgesan<sup>®</sup>, Epsom salts, magnesia, magnesium aluminum sulfite, magnesium aspartate, magnesium carbonate, magnesium chloride, magnesium citrate, magnesium diglycine, magnesium disuccinate hydrate, magnesium gluconate, magnesium glycerophosphate, magnesium glycinate, magnesium hydroxide, magnesium lactate, magnesium malate, magnesium murakab, magnesium orotate, magnesium oxide, magnesium phosphate, magnesium pidolate, magnesium salicylate, magnesium sulfate, magnesium trisilicate, milk of magnesia, Slo-Mag<sup>®</sup>, Super Malic<sup>®</sup>.

### Scientific evidence for common/studied uses:

Indication	Evidence Grade	 Grading System
Pre-eclampsia (and eclampsia)	A	
Arrhythmia	B	
Asthma	B	
Diabetes (type 2)	B	
Hearing loss	B	
Neuroprotection (for premature infants)	B	

### Brief Safety Summary:

- Likely safe:** When used orally, intravenously, or intramuscularly in people with normal renal function. Oral magnesium has been given in doses of 600-1,200mg daily for four months without major adverse effects. Higher doses of magnesium have been administered intramuscularly (IM) and intravenously for durations of 1-3 days. An initial loading dose is followed by a maintenance dose. Serum magnesium levels should be monitored in these situations. A common loading intramuscular dose is 8-10g; a common initial intravenous dose is a 4g bolus. The loading dose is followed by 1-3g intravenously per hour or a comparable IM dose repeated at longer intervals. The intravenous route is preferable to the IM route in most instances, because the intravenous dosage can be much more accurately titrated, and IM magnesium produces muscle tenderness at the injection site.
- Possibly unsafe:** According to secondary sources, hypermagnesemia may produce a number of symptoms, including thirst, hypotension, drowsiness, loss of tendon reflexes, muscle weakness, respiratory paralysis, cardiac arrhythmias, cardiac arrest, coma, and death. When magnesium sulfate is used topically for prolonged periods or repeatedly, as it may cause skin damage, based on case reports. When used in patients with bleeding disorders or hypotension or in those taking anticoagulant or antiplatelet agents, antidiabetic agents, antihypertensives, or antibiotics such as fluoroquinolones and cephalosporins, based on clinical research. When used in patients with decreased skeletal muscle tone, as, based on clinical research, magnesium may decrease skeletal muscle tone.
- Likely unsafe:** When used in patients with compromised renal function (plasma creatinine >300mcM/L) or atrioventricular heart block, based on clinical research. When used as a laxative in patients with gastrointestinal disorders, such as obstruction or ileus, based on secondary sources. When intravenous magnesium is used in women with toxemia during the first few hours of labor, based on secondary sources. When high intravenous doses of magnesium are administered to pregnant women for eclampsia, pre-eclampsia, or tocolysis (labor prevention), as a meta-analysis has reported an increase in infant mortality. When used in patients with known allergy/hypersensitivity to magnesium or other products found in magnesium supplements,

although magnesium allergy is reported to be extremely rare.

## Omega-3 fatty acids, fish oil, alpha-linolenic acid

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### Synonyms/Common Names/Related Substances:

ALA, alpha-linolenic acid (ALA, C18:3n-3), cod liver oil, coldwater fish, DHA, docosahexaenoic acid (DHA, C22:6n-3), docosapentaenoic acid (DPA, 22:5n-3), DPA, eicosapentaenoic acid (EPA, C20:5n-3), EPA, fish body oil, fish extract, fish liver oil, fish oil fatty acids, halibut oil, long-chain polyunsaturated fatty acids, Lovaza®, mackerel oil, marine oil, MaxEPA®, menhaden oil, n-3 fatty acids, n-3 polyunsaturated fatty acids, Omacor®, Omegaven®, omega fatty acids, omega-3 fatty acids, omega-3 oils, polyunsaturated fatty acids (PUFA), salmon oil, seal oil, shark liver oil, w-3 fatty acids.

Note: This professional monograph is based on a search of omega-3 fatty acids, and not the individual omega-3 fatty acids. Additional professional monographs are available on DHA, EPA, fish oil, and alpha-linolenic acid (ALA). Omega-3 fatty acids should not be confused with omega-6 fatty acids.

### Scientific Evidence for Common/Studied Uses:

Indication	Evidence Grade	 Grading System
Coronary heart disease	A	
Hyperlipidemia (triglyceride lowering)	A	
Hypertension	A	
Rheumatoid arthritis (fish oil)	A	
Secondary cardiovascular disease prevention (fish oil / EPA plus DHA)	A	
AIDS/HIV	C	

### Brief Safety Summary

- Likely Safe:** When taken as a supplement in recommended doses for limited duration (up to 2-3.5 years) or when incorporated into the diet (1-2 fish meals per week) continuously. The U.S. Food and Drug Administration has ruled that the use of eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), the primary omega-3 fatty acids found in fish, as dietary supplements is safe and lawful, provided that daily intakes of EPA and DHA omega-3 fatty acids do not exceed 3g per person daily from conventional food and dietary supplement sources.
- Possibly Safe:** When used orally in amounts found in foods during pregnancy and lactation; there is insufficient reliable information available about the safety of fish oils when used in amounts greater than those found in foods during pregnancy and breastfeeding. Up to 20g of fish may be well tolerated by most adults, although some experts recommend against this dose due to the theoretical risk of bleeding complications. DHA supplementation (50mg/kg daily for six months) of cystic fibrosis patients was not associated with adverse development or intolerance.
- Possibly Unsafe:** When used in patients with bleeding disorders or those using anticoagulants or antiplatelets, due to an increased risk of bleeding, particularly at doses of 3g daily or greater. There are case reports of increased bleeding and elevated international normalized ratios (INR) in patients taking warfarin with fish oil. When used in diabetic patients, as slight increases in fasting blood glucose levels have been noted in patients with type 2 diabetes. Though the available scientific evidence suggests that there are no statistically significant long-term effects

of fish oil in patients with diabetes, including no changes in hemoglobin A1c levels, limited reports in the 1980s of increased insulin needs in diabetic patients taking long-term fish oils may be related to other dietary changes or weight gain. When used in patients with low blood pressure or those using hypotensive agents, as omega-3 fatty acids have been found to cause reductions in blood pressure. Increases in LDL cholesterol have been observed with intake of omega-3 fatty acids. Extended ingestion of fish oil may cause a deficiency of vitamin E. When used in individuals at risk for hormone imbalance or those undergoing hormone replacement therapy, as decreased estrogen receptor production has been associated with fish oil supplementation. When used in patients with ventricular tachycardia or ventricular arrhythmia, due to worse outcome in omega-3 supplemented tachycardia and arrhythmia patients. When used in patients with asthma, based on a report of exacerbation of asthma in one subject. When used in patients with inflammatory bowel disease, as worsening of ulcerative colitis was reported in one subject in a clinical trial. When used in patients with liver disease or those using hepatotoxic agents, as mild elevations in liver function tests (alanine aminotransferase) have been reported. When used in patients at risk for colon cancer. According to preliminary evidence, fish oils may further increase the risk of colon cancer in individuals with familial adenomatous polyposis (FAP): three patients with a preexisting diagnosis of FAP were found to have malignant lesions during a course of long-term fish oil therapy. However, given the high risk for the development of colon cancer in patients with FAP, the specific role of fish oil in mediating risk of malignancy is not clear. Caution is warranted with the intake of large amounts of fish oil as vitamin A and D toxicity may occur.

- **Likely Unsafe:** Avoid in patients with known allergy or hypersensitivity to fish, fish oil, or omega-3 fatty acid products derived from fish.

## Selenium (Se)

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### Synonyms/Common Names/Related Substances:

5-Methylselenocysteine, adrusen zinco, atomic number 34, DL-selenomethionine, ebselen (2-phenyl-1,2-benzisoselenazol-3(2H)-one), gamma-glutamyl-selenomethyl-SeCys, high-selenium yeast, L-selenomethionine, methylseleninic acid, methyl selenol, monomethylated Se, MSC, Na<sub>2</sub>SeO<sub>3</sub>, parselenium, Se, Se-EMP, selen, selenate, selenious acid, selenite, selenite-exchangeable metabolic pool, selenium, selenium dioxide, selenium disulfide, selenium sulfide, selenium-enriched wheat, selenium-enriched yeast, selenium-rich pea flour, selenium-zinc, selenized yeast, seleno yeast, selenocysteine, selenoenzymes, seleno-L-methionine, selenomethionine (Semet), selenomethyl-SeCys, selenoprotein P, selenoproteins, selenous acid, Sele-Pak, selepen, Selmevit, Se-malt, SeMCYS, Seme, SeMet, Se-methylselenocysteine, SeO<sub>3</sub>(2-), SeO<sub>4</sub>(2-), SeS, se-spirulina, Se-yeast, se-yeast, SLM, sodium selenate, sodium selenite (Na<sub>2</sub>SeO<sub>3</sub>), Spirulin-Sochi-Selen, wheat selenium.

Selected combination products: Selmevit.

### Scientific Evidence for Common/Studied Uses:

Indication	Evidence Grade	 Grading System
Antioxidant	B	
Keshan disease	B	
Prostate cancer prevention	B	
HIV/AIDS	C	

### Brief Safety Summary:

- Likely Safe:** When used orally in amounts up to 200mcg daily or 100mcg daily. When used orally in amounts up to 5mcg daily as short-term enteral supplementation in preterm infants. Selenomethionine may be escalated safely to 7,200mcg twice daily for one week, followed by 7,200mcg once daily in combination with a standard dose of irinotecan. Currently, doses below the tolerable upper intake level (400mcg) may be used in supplementation. It has been suggested that the mean selenium intake (800mcg [10mcM] daily) represents a no-observed-adverse-effects level (NOAEL), while 600mcg (7.6mcM) daily of selenium intake was the lower 95 percent confidence limit for the NOAEL. High-selenium yeast and celecoxib may be taken in patients with cancer at the described doses, with minimum short-term negative effects.
- Possibly Unsafe:** When used in doses from 27-2,310mg daily. It has been suggested that 913mcg (12mcM) of selenium intake daily represents an individual marginal toxic daily selenium intake or lowest-observed-adverse-effects level (LOAEL). Blood levels can be used to assess toxicity. Levels below 1,000mcg/L were not associated with serious damage. Levels above 2,000mcg/L were predictive of serious damage. Normal serum levels range from 46 to 143mcg/L. When used in patients on hemodialysis, as concomitant administration of erythropoietin (EPO) and selenium may increase whole blood and plasma selenium levels in these patients. When used in patients with iodine deficiency, as hypothyroidism has been reported as a result of selenium supplementation. When used in patients with hyperlipidemia, as high serum selenium

concentrations have been associated with increased total and LDL cholesterol. When used in patients with immune disorders or those using immunosuppressants, based on *in vitro*, animal, and human research that has shown that selenium stimulates the immune system via cellular and humoral immunity. When used in patients using corticosteroids, as, based on human research, these agents may lower plasma selenium levels. When used in patients using antacids, as, based on secondary sources, antacids may reduce the absorption of selenium. When used in patients using erythropoietin (EPO), as, based on human research, selenium may increase the effects of EPO. When used in patients using HMG-CoA reductase inhibitors ("statins"), as, based on human research, selenium may reduce the effectiveness of these agents. When used in patients using oral contraceptives, as, based on human research, these agents may reduce selenium levels. When used in patients using astragalus, as, based on research, astragalus may cause selenium to accumulate; theoretically, concurrent use of astragalus with selenium may increase the risk of selenium toxicity. When used in patients taking iron supplements, as, based on human research, serum selenium levels may be affected by iron supplementation; iron-deficiency anemia does not appear to alter serum selenium or glutathione peroxidase concentrations.

- **Likely Unsafe:** When used in patients at high risk of nonmelanoma skin cancer, as selenium supplementation has been shown to increase the risk of squamous cell carcinoma and total nonmelanoma skin cancer; however, other research has not found an increased incidence. When used in patients at risk for developing diabetes, as selenium supplementation may increase risk for type 2 diabetes. When used in patients with known allergy/hypersensitivity to products containing selenium; however, selenium is a trace element, and hypersensitivity is unlikely.

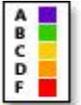
## Vitamin B12

*Natural Standard Professional Monograph, Copyright © 2012 (www.naturalstandard.com).*

### Synonyms/Common Names/Related Substances:

Adenosylcobalamin, AdoB12, B complex, B complex vitamin, B-12, bedumil, cobalamin, cobalamins, cobamin, cyanocobalamin, cyanocobalamine, cyanocobalaminum, cycobemin, hydroxocobalamin, hydroxocobalaminum, hydroxocobemine, idrossocobalamina, methylcobalamin, vitadurin, vitamin B-12, vitamina B12 (Spanish), vitamine B12 (French).

### Scientific Evidence for Common/Studied Uses:

Indication	Evidence Grade	 Grading System
Megaloblastic anemia - due to vitamin B12 deficiency	A	
Vitamin B12 deficiency	A	

### Brief Safety Summary:

- Likely safe:** When used orally in doses not exceeding the recommended dietary allowance (RDA).
- Possibly unsafe:** When used in patients with cardiovascular concerns, as, in clinical research, an intravenous loading dose of folic acid, vitamin B6, and vitamin B12, followed by daily oral administration after coronary stenting, increased restenosis rates. When used in patients with elevated blood pressure, as hypertension following intravenous administration of hydrocobalamin has been reported in clinical studies. When used in patients with dermatologic concerns, as pustular or papular rash, erythema at the injection site, and pruritus have been reported in clinical research. Vitamin B12 and pyridoxine together have been associated with cases of rosacea fulminans, characterized by intense erythema with nodules, papules, and pustules. Symptoms may persist for up to four months after the supplement is stopped and may require treatment with systemic corticosteroids and topical therapy. Pink or red skin discoloration has also been reported. When used in patients with genitourinary concerns, as chromaturia has been reported in clinical studies. When used in patients with gastrointestinal concerns, as nausea and dysphagia have been reported in clinical studies. According to secondary sources, diarrhea has also been reported. When used in patients with hematological concerns, as, according to case report data, treatment of vitamin B12 deficiency may lead to polycythemia vera, which is characterized by an increase in blood volume and the number of red blood cells. When used in patients with subnormal serum potassium levels, as, according to case report data, the correction of megaloblastic anemia with vitamin B12 may result in fatal hypokalemia in susceptible individuals. When used in patients with a history of gout or elevated uric acid levels, as the correction of megaloblastic anemia with vitamin B12 may precipitate gout in susceptible individuals. When used in patients taking the following agents, as they have been associated with reduced absorption or reduced serum levels of vitamin B12: ACE inhibitors, acetylsalicylic acid (aspirin), antibiotics, anticonvulsants, bile acid sequestrants, colchicine, H2 blockers, metformin, neomycin, nicotine, nitrous oxide, oral contraceptives, para-aminosalicylic acid, potassium chloride, proton pump inhibitors (PPIs), and zidovudine (AZT, Combivir®, Retrovir®). Additionally, preliminary evidence suggests that vitamin C may cause degradation of vitamin B12 in multivitamin supplements and that chloramphenicol may inhibit the biosynthesis of vitamin B12.

- **Likely unsafe:** When used in patients sensitive or allergic to cobalamin, cobalt, or any other vitamin B12 product ingredients.

## Vitamin C (ascorbic acid)

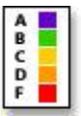
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### Synonyms/Common Names/Related Substances:

Acide ascorbique (French), acide cévitamique (French), acide iso-ascorbique (French), acide L-ascorbique (French), ácido ascórbico (Spanish), antiscorbutic vitamin, ascorbate, ascorbate de calcium, ascorbate de sodium, ascorbic acid (AA), ascorbyl palmitate, calcium ascorbate, cevitamic acid, iso-ascorbic acid, L-ascorbic acid, magnesium ascorbate, palmitate d'ascorbyl (French), selenium ascorbate, sodium ascorbate, vitamina C (Spanish), vitamine antiscorbutique (French), vitamine C (French).

Note: Due to the large number of studies on the effects of vitamin C, meta-analyses and systematic reviews are the primary focus for this monograph.

### Scientific Evidence for Common/Studied Uses:

Indication	Evidence Grade	 Grading System
Vitamin C deficiency (scurvy)	A	
Common cold prevention (extreme environments)	B	
Iron absorption enhancement	B	
Urinary tract infection (during pregnancy)	B	
HIV (transmission)	C	

### Brief Safety Summary:

- Likely safe:** Vitamin C is generally regarded as safe in amounts normally obtained from foods. Vitamin C supplements are also generally regarded as safe in most individuals in recommended amounts, although side effects are rarely reported, including nausea, vomiting, heartburn, abdominal cramps, and headache.
- Possibly unsafe:** When used orally in excessive amounts. The tolerable upper intake level (UL) is 400mg daily for children 1-3 years old, 650mg daily for children 4-8 years old, 1,200mg daily for children 9-13 years old, and 1,800mg daily for adolescents 14-18 years old. High doses of vitamin C have been associated with multiple adverse effects, including kidney stones, severe diarrhea, nausea, and gastritis, according to secondary sources. Flushing, faintness, dizziness, and fatigue have also been noted. Parenteral (injected) vitamin C may cause dizziness, faintness, or injection site discomfort, and in high doses, it may lead to renal insufficiency. Dental erosion may occur from chronically chewing vitamin C tablets. Healthy adults who take chronic large doses of vitamin C may experience low blood levels of vitamin C when they stop taking the high doses and resume normal intake, according to secondary sources. Although rare, scurvy may result, due to tolerance or resistance following cessation after long-term, high-dose use, such as in infants born to mothers taking extra vitamin C throughout pregnancy, according to secondary sources. When used in patients with diabetes, as vitamin C may affect glycogenolysis and increase blood sugar, according to secondary sources. In postmenopausal women with diabetes, in doses greater than 300mg daily, it has been associated with an increased risk of cardiovascular mortality. When used in patients after angioplasty, due to the potentially harmful effects of antioxidant vitamins. When used in patients with cancer, as cancer cells may accumulate high doses of vitamin C, according to secondary sources. However, it is unknown if this effects is harmful. When used in patients with glucose-6-phosphate dehydrogenase deficiency, as large amounts of vitamin C may cause hemolysis in these individuals. When used

in patients with anemia and related conditions, or in those taking iron supplements, as vitamin C has been shown to increase iron absorption. When used in patients with kidney stones, as large amounts of vitamin C may increase the risk of stone formation. When used in patients with sickle cell disease, as vitamin C may decrease blood pH, according to secondary sources. When used in patients who are taking antibiotics, due to the possibility of the decreased efficacy of the antibiotic when taken with vitamin C. When used in patients taking antiplatelets or anticoagulants, as vitamin C may interfere with the blood-thinning effects of these agents. When used in patients taking antineoplastics, as vitamin C may antagonize the effects of reactive oxygen species-generating antineoplastic drugs, due to its antioxidant properties, according to secondary sources. When used in patients taking HIV medications, as, in humans, concomitant administration of high doses of vitamin C and the protease inhibitor indinavir may reduce steady-state indinavir plasma concentrations. When used in patients taking barbiturates, as, in mice, pharmacological doses of ascorbic acid prolonged the effects of pentobarbital anesthesia. When used in patients taking estrogens, as oral estrogens may decrease the effects of vitamin C in the body. When used in patients taking fluphenazine, as vitamin C supplementation may decrease levels of the drug fluphenazine in the body.

- **Likely unsafe:** When used in patients with a known allergy/hypersensitivity to any of the ingredients in vitamin C products. When high doses of vitamin C are used in people with conditions aggravated by acid loading, such as cirrhosis, gout, renal tubular acidosis, or paroxysmal nocturnal hemoglobinuria, according to secondary sources. When high doses of vitamin C are used in patients with kidney failure or in those taking agents that may damage the kidneys, due to an increased risk of kidney failure.

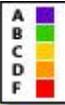
## Vitamin D

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### Synonyms/Common Names/Related Substances:

1,25-DHCC, 1,25-dihydroxy-22-ovavitamin D(3), 1,25-dihydroxycholecalciferol, 1,25-dihydroxy-vitamin-D (1,25(OH)(2)D), 1,25-dihydroxyvitamin D3, 1,25-diOHC, 1,25(OH) 2D3, 1-alpha (OH) D3, 19-nor-1, 1-alpha-hydroxycholecalciferol, 1-alpha-hydroxyvitamin D2, 1-hydroxyvitamin D, 22-oxacalcitriol (OCT), 24,25(OH)(2)vitamin D(3), 25 hydroxyvitamin D (25(OH)D), 25-dihydroxyvitamin D2, 25-dihydroxyvitamin D2, 19-nor-1, 25-HCC, 25-hydroxycholecalciferol, 25-hydroxyvitamin D, 25-hydroxyvitamin D3, 25-OHCC, 25-OHD3, activated 7-dehydrocholesterol, activated ergosterol, alfalcidol, calcifediol, calcipotriene, calcipotriol, calcitriol, cholecalciferol, colecalciferol, cod liver oil, dichysterol, dihydrotachysterol, dihydrotachysterol 2, doxercalciferol, ecocalcidiol, ED-21 (vitamin D analog), ED-71 (vitamin D analog), ergocalciferol, ergocalciferolum, falecalcitriol, hexafluoro-1,25dihydroxyvitamin D3, irradiated ergosterol, maxacalcitol, MC903, Ostelin®, paracalcin, paricalcitol, tacalcitol, Vi-delta Liquid emulsion®, viosterol, vitamin D2, vitamin D3, vitamina D.

### Scientific Evidence for Common/Studied Uses:

Indication	Evidence Grade	 Grading System
Familial hypophosphatemia	A	
Fanconi syndrome-related hypophosphatemia	A	
Hyperparathyroidism due to low vitamin D levels	A	
Hypocalcemia due to hypoparathyroidism	A	
Osteomalacia (adult rickets)	A	
Psoriasis (vitamin D analogs)	A	
Rickets	A	
Vitamin D deficiency	A	
Dental caries	B	
Fall prevention	B	
Muscle weakness/pain	B	
Osteoporosis (general)	B	
Renal osteodystrophy	B	

### Brief Safety Summary:

- Likely safe:** When using 100mcg of vitamin D3 daily (4,000 IU) and when used topically for skin conditions like vitiligo, alone or in combination with topical corticosteroids, for up to three months.
- Possibly safe:** When using 300,000 IU of vitamin D2 or D3 orally or intramuscularly three times a year for vitamin D insufficiency.
- Possibly unsafe:** When used in patients with cardiovascular disease, as treatment with vitamin D analogs was related to coronary and vascular calcification, a combination of calcium and vitamin D significantly increased the risk of myocardial infarction and stroke in a meta-analysis, and in human research, vitamin D lacked an effect on total cholesterol or triglycerides; however, LDL

cholesterol levels increased overall and HDL cholesterol levels decreased in studies lasting longer than one year. When used in patients with skin disorders, due to reports in clinical research of contact dermatitis, skin irritation, and rash and skin atrophy. When used in patients with liver disease, as vitamin D is metabolized in the liver. When used in patients with diabetes or those using hypoglycemic agents, as, according to a clinical review and human research, the effects of vitamin D on glucose and insulin metabolism are mixed, with studies showing reduced effects or no effects and in a single study included in one of the reviews, healthy men had significantly increased insulin and C-peptide concentrations. When used in patients with gastrointestinal disorders, as, according to secondary sources and case reporting, high amounts of vitamin D may cause gastrointestinal complaints, and constipation and gastric symptoms such as diarrhea, abdominal cramps, vomiting, and upset stomach have been reported in clinical research. When used in patients with hypotension or hypertension, or in those using agents that affect blood pressure, as, according to systematic review and secondary sources, vitamin D supplementation resulted in a reduction in blood pressure in most studies; however, increases were noted in a single study and there was a lack of effect in separate studies. When used in patients with hyperparathyroidism, as vitamin D may increase calcium levels. When used in patients with musculoskeletal disorders, as, despite its popular use to prevent falls, some researchers have noted that vitamin D may result in more falls and fractures and musculoskeletal soreness and pain have been reported. When used in individuals at risk of headaches, as headaches have been reported in clinical trials. When used in patients at risk of respiratory disorders, as increased upper respiratory tract infections have been reported in clinical trials. When used in patients with renal disease, as vitamin D may increase calcium levels and the risk of arteriosclerosis; also, vitamin D use has been associated with an increased risk of renal or urinary tract stones, and use has possibly been associated with renal calculi. When used in patients with granulomatous disorders (sarcoidosis, tuberculosis, fungal granulomas, berylliosis, and lymphomas), which are associated with calcium metabolism disorder, as theoretically, concurrent use of high amounts of vitamin D in these patients may increase the risk of hypercalcemia and kidney stones. When used in pregnant women at risk of gestational hypertension, as, according to a systematic review, 600-800 IU of vitamin D significantly reduced pre-eclampsia risk vs. <200 IU daily; however, the risk of gestational hypertension increased. When used in mothers who are receiving vitamin D supplements and are breastfeeding, as, according to human research, vitamin D supplementation during breastfeeding may increase the risk of urinary tract infection, particularly in the first three months.

- **Likely unsafe:** When used in individuals with known allergy to vitamin D, any of its analogs and derivatives, or any component of the formulation or with vitamin D hypersensitivity syndromes. When used in individuals with hypercalcemia or hypercalciuria, as, in human research, vitamin D supplementation has caused hypercalcemia and hypercalciuria, particularly at high doses.

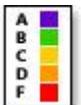
## Whey protein

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### Synonyms/Common Names/Related Substances:

2-Methyl butanal, 3-methyl butanal, 39kDa protein, acid whey protein, alpha-lactalbumin, alpha-lactorphin, amino acids, antioxidant, apolipoprotein H-like whey protein, beta-lactoglobulin A, beta-lactoglobulin B, beta-lactoglobulin isoform A, beta-lactoglobulin isoform B, bovine serum albumin (BSA), bovine transferrin, bovine whey protein concentrate, branched-chain amino acids, calcium, calmodulin, casein, cathepsin D, CD14, cheese, cheese whey, copper, cottage cheese whey, cysteine, denatured lactoperoxidase, dimethyl sulfide, early lactation protein, Enhanced Life Extension Protein, EquiPro™, FIL (Feedback inhibitor of Lactation), folacin-binding protein, Fonterra™, furosine, globular protein, glutathione, goat milk whey, goat whey, glycemic index lowering peptide fraction (GILP), glycolactin, glycomacropeptide (GMP), glycoprotein PP3, glycosylated bile salt-stimulated lipase (BSSL), HMS90™, hormones, IgG1, IgG2, IgG rich fractions, Immune WPC-40™, Immunocal™, immunoglobulins, Lactermin™, lactoferrin, lactoperoxidase, lactophorin, late-lactation protein, leucine, lysinoalanine, lysozyme, magnesium, MBP, methional, milk, milk basic protein, milk constituent, milk protein, milk protein isolate, milk proteose peptone-3, mineral whey concentrate, MUC15, NOP47, Optimune™, Peptamen®, phosphate, phosphorylated beta-lactoglobulin, phosphorylated whey, Prolibra™, prosaposin, protein N-linked homocysteine, proteínas del suero de la leche (Spanish), PROther®, ProtherSOD®, salty whey, selenium, serum albumin, sialic acid, sweet whey, transforming growth factor-beta-2 (TGF-beta-2), trichosurin, undenatured whey protein, vitamin B12, WE80BG, WGP-88, whey, whey acidic protein, whey fraction, whey growth factor extract, whey peptides, whey permeate, whey protein concentrate, whey protein hydrolysate, whey protein isolate, whey proteine, zinc.

### Scientific Evidence for Common/Studied Uses:

Indication	Evidence Grade	 Grading System
Allergies (prevention)	A	
Nutritional supplement (protein source)	A	
Appetite suppressant	B	
Diabetes	B	
Enhanced muscle mass / strength	B	
Weight loss	B	
HIV	C	

### Brief Safety Summary:

- **Likely safe:** Whey protein is likely safe for most adults when used in manufacturer-recommended amounts. There is a general lack of reported adverse effects in nonallergic persons.
- **Possibly safe:** When up to 50g of whey protein as a single dose is used. When up to 30g of whey protein is used daily for six months.
- **Possibly unsafe:** When used in patients using medications, according to secondary sources suggesting that whey protein can affect the pharmacokinetic response of some medications. When used in patients with diabetes or patients using blood sugar-lowering medications, due to

the potential for decreases in blood glucose and increases in insulin, as shown in human studies. When used in patients using blood cholesterol-lowering medications, due to the potential alteration of lipid levels, according to human and animal research. When used in patients using antithrombotic agents, as, in *in vitro* research, unheated and heat-denatured alpha-lactalbumin and denatured beta-lactoglobulin stimulated plasminogen activator activity. When used in patients using medications metabolized by cytochrome P450 enzymes, as, in animal research, the level of CYP1A2 mRNA was reduced when animals were fed whey vs. casein. This was accompanied by a reduction in constitutive levels of the Ah receptor in liver cytosol. When used in patients with low blood pressure or those using hypotensive medications, as, in human research, hydrolyzed and nonhydrolyzed whey protein reduced blood pressure. When used in patients using immunomodulating agents, as, in human research, serum response to a vaccine was higher with whey protein vs. soy protein; in animal and human research, whey protein has been shown to affect immunoglobulin levels. When used in patients with gastrointestinal disorders, as gastrointestinal side effects were reported in clinical trials. When operating heavy machinery since, as, according to secondary sources, high doses of protein may cause tiredness or fatigue.

- **Likely unsafe:** When used in patients with known allergy or hypersensitivity to milk or milk products. When used long-term and in excessive amounts, according to information from secondary sources suggesting that protein used in this manner may be associated with deteriorating kidney function and possibly osteoporosis. When used in individuals avoiding dairy products, due to concern about developing diabetes, according to information from secondary sources suggesting that certain proteins in milk may contribute to the development of diabetes in children.

**Note:** Use only approved sources of whey protein or whey protein hydrolysates in infant formulas.

## Ungraded Supplements

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Fiber

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Meal Replacements (Ensure/Glucerna)

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Multivitamin

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## *Attachments*

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HCPH RWGA Grants Management

MEDICAL NUTRITIONAL THERAPY PROGRAM

REQUEST TO ADD SUPPLEMENT TO APPROVED FORMULARY

Advance Approval Required - All sections must be completed. Printed or Typewritten responses only

NAME OF CONTRACTOR:	
SERVICE:	FUND:
CONTRACT NO:	CONTRACT TERM:

FORMULARY ADDITION REQUEST:

SUPPLEMENT NAME:	
APPROXIMATE COST:	

JUSTIFICATION (Please provide a detailed description of how the supplement is related to the treatment of HIV. At least two evidence-based peer-reviewed journal articles must be included with submission):

By: \_\_\_\_\_  
 Clinician Name                      Licensure                      Signature                      Date  
 Must be approved by applicable Agency clinician (MD, DO, NP, PA, Pharmacist)

Submit to RWGA Grants Management via fax (713) 439-6338 or email [hivacct@hcphe.org](mailto:hivacct@hcphe.org)

(Submitted by)  
 Name (print) \_\_\_\_\_ Fax # \_\_\_\_\_ Phone # \_\_\_\_\_  
 Signature \_\_\_\_\_ Email \_\_\_\_\_ Date \_\_\_\_\_

All formulary addition requests will be reviewed for approval quarterly by the Clinical Quality Management Committee

APPROVED                       DISAPPROVED

\_\_\_\_\_  
 Manager, Ryan White Grant Administration (RWGA)                      Date