

**FAMILY** 

CAUTION: See separate listings for Vitamin A and for other carotenoids, such as Astaxanthin and Lutein.

#### ∧ Other Common Names

A-Beta-Carotene, A-Bêta-Carotène, Bêta-Carotène, Bêta-Carotène Tout Trans, Beta-Caroteno, Carotenes, Carotènes, Carotenoids, Caroténoïdes, Caroténoïdes Mélangés, Mixed Carotenoids, Provitamin A, Provitamin A.

## Overview

Beta-carotene is a pigmented, fat-soluble compound called a carotenoid. Carotenoids are dietary precursors to vitamin A and are converted to vitamin A in the body (7135). Beta-carotene is found in green leafy and orange vegetables, some fruit, and some tree nuts (34490,34617). Like other carotenoids, beta-carotene is considered to be an antioxidant (93095).

The American Heart Association recommends obtaining beta-carotene and other antioxidants from a diet high in fruits, vegetables, and whole grains rather than through supplements (1440). Similar statements have been released by the American Cancer Society, the World Cancer Research Institute in association with the American Institute for Cancer Research, and the World Health Organization's International Agency for Research on Cancer (1470).

#### Safety

LIKELY SAFE ...when used orally and appropriately. Beta-carotene supplements are appropriate for certain specific conditions; however, beta-carotene supplementation is not recommended for the general population (4844,6393). There is no tolerable upper intake level (UL) set for beta-carotene. However, doses as low as 20 mg/day have been associated with increased risk of lung and prostate cancer in people who smoke (1371,3359,3937,3959,6393,11786). There is also concern that taking high doses of antioxidants such as beta-carotene might do more harm than good. In several analyses of clinical studies involving smokers and healthy non-smokers, taking beta-carotene supplements alone or in combination with other antioxidants is associated with an increased risk of mortality from all causes (15305,34514,90775).

POSSIBLY UNSAFE ...when used orally in high doses or in people who smoke or have a history of asbestos exposure. Supplemental beta-carotene 20 mg daily for 5-8 years seems to increase the risk of lung cancer, prostate cancer, intracerebral hemorrhage, and cardiovascular and total mortality in people who smoke cigarettes or have a history of high-level exposure to asbestos (1371,3359,3937,3959,6393,11786,34591). There is also concern that taking high doses of antioxidants such as beta-carotene might do more harm than good in the general population. In several analyses of clinical studies involving smokers and healthy non-smokers, taking beta-carotene supplements alone or in combination with other antioxidants is associated with an increased risk of mortality from all causes (15305,34514,90775).

Beta-carotene from foods does not seem to have this effect.

CHILDREN: LIKELY SAFE ...when used orally and appropriately (4844). High doses (greater than 60 mg per day) have been used with apparent safety for specific conditions such as erythropoietic protoporphyria (11793).

PREGNANCY AND LACTATION: LIKELY SAFE ...when used orally and appropriately (4844,6393). There is insufficient reliable information available about the safety of large doses of beta-carotene in pregnancy and lactation.

## **∧** Adverse Effects

General: Orally, beta-carotene is well-tolerated when used in appropriate amounts.

## Most Common Adverse Effects:

Orally: Belching, orange skin (temporary).

### Serious Adverse Effects (Rare):

Orally: Increased cardiovascular mortality and cancer risk in smokers and other specific patient populations.

### ▲ Cardiovascular

Orally, beta-carotene 20 to 30 mg daily seems to increase cardiovascular mortality by 12% to 26% in people who smoke (2642,3949,108641). Smokers and people with a history of asbestos exposure should not use beta-carotene supplements. In males who smoke and have had a prior myocardial infarction (MI), the risk of fatal coronary heart disease increases by as much as 43% with beta-carotene 20 mg daily (3937). These adverse effects do not seem to occur in people who eat foods high in beta-carotene content (1440,2657).

## ▲ Dermatologic

High oral doses of beta-carotene in foods or supplements can cause yellow or orange skin pigmentation called carotenoderma (11786,34572,34594,91382,108641). In clinical trials, the incidence of carotenoderma has been reported to be up to 15.8% (34626).

### **∧** Gastrointestinal

Orally, beta-carotene may cause belching (34572,34594).

#### ∧ Ocular/Otic

In a case report, treatment with a high dose of beta-carotene and canthaxanthin for more than 6 years resulted in the development of glistening bright yellow crystalline deposits around the maculae. This resulted in a slight decrease in visual acuity and adaptation to the dark (34641).

## ∧ Oncologic

Smokers and people with a history of asbestos exposure should not use beta-carotene supplements. Beta-carotene in doses of 20 mg per day for 5-8 years has been associated with an increased risk of lung and prostate cancer and increased total mortality in people who smoke cigarettes (21 or more daily), and in people with a history of high-level asbestos exposure (3959,6393,11303,11786,104467,108641). These adverse effects do not seem to occur in people who eat foods high in beta-carotene content (1440,2657). There is also concern that beta-carotene might increase the risk of adverse outcomes in non-smokers. In one large-scale population study, males who took a multivitamin more than 7 times per week and who also took a separate beta-carotene supplement had a significantly increased risk of developing advanced prostate cancer (15607).

### ∧ Pulmonary/Respiratory

Clinical research shows that taking beta-carotene 20 mg daily, alone or along with vitamin E 50 mg daily, increases the risk of common colds by 21% to 25% in individuals participating in heavy exercise at leisure. However, it does not appear to affect the risk of common cold in individuals who participate in heavy activity at work (34508).

#### ^ Other

Analysis of studies in smokers and non-smokers suggests that taking beta-carotene supplements alone or in combination with other antioxidants increases the risk of mortality from all causes (15305).

## **≈** Effectiveness

#### **FFFFCTIVE**

Erythropoietic protoporphyria (EPP). Oral beta-carotene reduces photosensitivity in patients with EPP.

^ Details: Oral beta-carotene can reduce photosensitivity in patients with EPP, a genetic disorder resulting in defective porphyrin metabolism. In adults, beta-carotene 180-300 mg daily is used. In children 1-4 years old, the daily dose is 60-90 mg; 5-8 years, 90-120 mg; 9-12 years, 120-150 mg; 13-16 years, 150-180 mg; and 16 and older, 180 mg. If an adequate response is not obtained, beta-carotene can be increased by 30-60 mg per day for children under 16 years, and up to a maximum of 300 mg per day for children 16 years and older (11793,34455,34651,34652,34653,34673).

# POSSIBLY EFFECTIVE

Breast cancer. A diet rich in beta-carotene modestly reduces breast cancer risk.

^ Details: Observational research has found that a diet rich in beta-carotene is associated with reduced risk of breast cancer in premenopausal adults, especially those at high risk due to family history or high alcohol intake (1444,10132). Other observational research has also found that increased beta-carotene intake is associated with up to an 18% decreased risk of breast cancer and up to a 30% increased overall survival in breast cancer patients (10824,101697).

Postpartum complications. Taking beta carotene orally seems to reduce the occurrence of postpartum diarrhea, fever, night blindness, and mortality in malnourished patients.

^ Details: A large clinical study in pregnant patients in Nepal shows that taking all-trans beta-carotene (synthetic beta-carotene) 42 mg weekly before, during, and after pregnancy reduces, but does not eliminate, the occurrence of postpartum diarrhea, fever, and night blindness when compared with placebo (2581). Further clinical studies in pregnant patients in Nepal show that taking the same dose of all-trans beta-carotene seems to reduce pregnancy-related mortality, but not fetal and early infant mortality, when compared with placebo (6152,6153,6154).

Sunburn. Oral beta-carotene seems to modestly reduce the risk for sunburn in sensitive individuals.

^ Details: A meta-analysis of multiple clinical studies suggests that beta-carotene must be taken for at least 10 weeks to have a protective effect against sunburn (34562). There is also some evidence that taking beta-carotene 25 mg, alone or as a mixture of beta-carotenoids, daily for 12 weeks reduces skin redness after exposure to UV light in sun-sensitive individuals (6134,34496). However, beta-carotene is unlikely to have much effect on sunburn risk in most people (11792). Also, it does not seem to reduce the incidence of solar keratoses or skin cancers associated with sun exposure (1297,2599,11302).

### POSSIBLY INEFFECTIVE

Aneurysm. Oral beta-carotene does not seem to reduce abdominal aneurysm risk.

△ Details: Clinical research shows that taking beta-carotene 20 mg daily does not reduce the incidence of abdominal aortic aneurysm in male smokers when compared to patients not taking beta-carotene after a follow-up period of 5.8 years (34462).

Alzheimer disease. Oral beta-carotene does not seem to reduce Alzheimer disease risk.

△ Details: Most research suggests that intake of dietary or supplemental beta-carotene does not seem to have any effect on Alzheimer disease risk (10131,34597,34624,90082).

Cataracts. Oral beta-carotene supplements do not seem to reduce the risk of cataract development.

^ Details: A meta-analysis of population research has found that the highest DIETARY intake of beta-carotene is associated with a modest 7% to 10% reduction in the risk of cataracts (90786,101699). However, taking beta-carotene SUPPLEMENTS does not seem to reduce the risk of cataracts. Clinical research and meta-analyses of clinical research show that taking beta-carotene

alone or in combination with vitamin C, vitamin E, and zinc for up to 8 years does not reduce the incidence of cataracts or the need for cataract surgery (7304,34626,101699).

Cystic fibrosis. Oral beta-carotene does not seem to improve lung function in patients with cystic fibrosis.

^ Details: A meta-analysis of clinical studies in patients with cystic fibrosis shows that taking beta-carotene orally 10-300 mg daily for up to 14 months does not improve lung function when compared with control (34605).

Diabetes. Oral beta-carotene does not seem to reduce the risk of developing diabetes or diabetic complications.

Details: Observational research has found inconsistent results regarding an association between dietary beta-carotene and the risk of developing type 2 diabetes (14004,34576,107292). However, one population study in patients with type 2 diabetes has found that an increased serum concentration of beta-carotene is associated with increased cardiovascular mortality over 14 years, with a 2.5-fold increased risk when the highest levels are compared with the lowest (109768).

Additionally, clinical research has been negative. One clinical study in females with a history of cardiovascular disease shows that taking beta-carotene 50 mg on alternate days does not prevent the development of type 2 diabetes when compared with placebo (34588). Another clinical study in males diagnosed with diabetes shows that taking beta-carotene 20 mg daily does not reduce the risk of macrovascular complications or mortality when compared with those not taking beta-carotene (34593).

Dysplastic nevi (atypical moles). Oral beta-carotene does not seem to reduce atypical moles.

^ Details: Clinical research in patients with numerous atypical moles shows that taking beta-carotene orally 50 mg daily for 36 months does not reduce the occurrence of newly developed moles when compared with placebo (34503).

Esophageal cancer. Oral beta-carotene does not seem to reduce esophageal cancer risk.

^ Details: While observational research suggests that consuming more beta-carotene in the diet reduces esophageal cancer, higher quality research does not agree (103675). Clinical research shows that taking beta-carotene and alpha-tocopherol supplements for 5-8 years does not reduce the incidence of upper digestive tract cancer, including esophageal cancer, in male smokers aged 50-69 years of age (34547). Additionally, a meta-analysis of low quality clinical research suggests that taking beta-carotene supplements alone or in combination with other antioxidants, such as vitamin A or vitamin E plus vitamin C, does not reduce the risk of esophageal cancer and may increase mortality (12185).

Liver cancer. Oral beta-carotene does not seem to reduce liver cancer risk.

^ Details: Clinical research in male smokers aged 50-69 years shows that taking beta-carotene 20 mg daily, alone or with vitamin E 50 mg daily, for 5-8 years does not reduce the incidence of liver cancer when compared with placebo (91383).

Liver disease. Oral beta-carotene does not seem to reduce mortality from liver disease in male smokers.

^ Details: Clinical research in male smokers aged 50-69 years shows that taking beta-carotene 20 mg daily alone or with vitamin E 50 mg daily for 5-8 years does not reduce the risk of mortality due to chronic liver disease when compared with placebo (91383).

Overall mortality. Oral beta-carotene does not seem to reduce all-cause mortality.

^ Details: Some meta-analyses published between 2007 and 2013 show that taking beta-carotene in doses of up to 50 mg daily or every other day, alone or in combination with other antioxidants, for up to 12 years increases the risk of overall mortality by 5% to 7% (15305,34622,90775). However, a more recent meta-analysis of clinical research shows that taking beta-carotene in doses up to 75 mg daily for up to 12 years does not affect the risk of overall mortality (109767). Additionally, some research shows that taking beta-carotene 6 mg daily in combination with vitamin C, vitamin E, selenium, and zinc for approximately 7 years might lower all-cause mortality in males, but not females (14109). It is unclear if any beneficial effects are related to beta-carotene, the other antioxidants, or the combination. With regard to dietary beta-carotene, a meta-analysis of population studies suggests that each 5000 mcg/day of increased intake is associated with an 8% reduction in mortality. In addition, each 25 mcg/dL increase in beta-carotene blood concentration is associated with a 19% reduction in mortality (109779).

Stroke. Oral beta-carotene does not seem to reduce stroke risk and may actually increase risk in some patients.

^ Details: Taking all-trans beta-carotene (synthetic beta-carotene) 20 mg daily orally for a median of 6 years does not reduce the overall incidence of stroke in male smokers (1371,34514). Additionally, there is some evidence that beta-carotene actually increases the risk of intracerebral hemorrhage by 62% in patients who also drink alcohol (1371,3359). However, evidence with dietary intake of beta-carotene is in contrast. A meta-analysis of population studies suggests that beta-carotene is associated with a 19% reduction in the risk of stroke per 5000 mcg/day of increased dietary intake and 15% reduction in risk of stroke per 25 mcg/dL increase in beta-carotene blood concentration (109779).

## LIKELY INEFFECTIVE

Cancer. Oral beta-carotene does not reduce the risk of most cancer types.

^ Details: The US Preventive Services Task Force (USPSTF) states that the harms of beta-carotene supplementation outweigh the potential benefits for prevention of cancer and therefore recommends against its use (108641,112166). Taking beta-carotene 20-50 mg daily, or 50 mg on alternate days, does not reduce the incidence of a variety of cancers in adults, including uterine, cervical, thyroid, bladder, skin (melanoma, basal cell carcinoma, squamous cell carcinoma), brain, and blood cancers (140,1297,1448,2599,2642,2646,2657,3949,34580,34612). Additionally, meta-analyses of multiple clinical studies show that beta-carotene supplementation does not decrease cancer-related mortality and can actually increase the risk of bladder cancer by 52% and lung cancer by 14% (34612,109767). Similarly, a meta-analysis of several population studies does not suggest that high versus low dietary beta-carotene intake is associated with reduced cancer risk. However, this analysis does suggest that each 25 mcg/dL increase in blood levels of beta-carotene is associated with a 24% lower risk of cancer (109779).

Cardiovascular disease (CVD). Oral beta-carotene does not reduce the risk of CVD, and supplementation may increase CVD-related mortality risk in some patients.

^ Details: The US Preventive Services Task Force (USPSTF) states that the harms of beta-carotene supplementation outweigh the potential benefits for prevention of CVD and therefore recommends against its use (108641,112166). Also, a Science Advisory from the American Heart Association states that the evidence does not justify use of antioxidants such as beta-carotene for reducing the risk of CVD (12142). Although large population studies of serum, dietary, or supplemental beta-carotene have found mixed effects of beta-carotene on CVD risk (3933,7386,7387,34566,101698,107290,109768,109779), most controlled clinical trials show either no effect or a negative effect on CVD incidence and/or mortality

(1448,2642,2646,2657,3935,3949,7388,9817,10130,14108,34552,34668). A meta-analysis of these and other randomized controlled trials in various populations shows that beta-carotene supplementation is associated with a modestly increased CVD incidence (109769). Meta-analyses also show that beta-carotene supplementation either increases CVD mortality or is not associated with CVD mortality (109767,109769). Some evidence suggests that the risk of CVD mortality is greatest in people who smoke

(2642,3937,3949). Most studies have used beta-carotene in doses of 20-50 mg daily or every other day, alone or in combination with other antioxidants (1448,2642,2646,2657,3935,3937,3949,7388,9817,10130,14108,34552,34668,109767,109769). The adverse effects of beta-carotene on CVD risk and/or mortality do not seem to occur in people who eat foods high in beta-carotene content (1440,2657,7714,7715,7716).

Colorectal adenoma. Oral beta-carotene supplementation does not reduce the risk of colorectal adenomas and may actually increase the risk in some patients.

^ Details: Most clinical studies show that taking beta-carotene 20-75 mg daily or 50 mg on alternate days does not decreas the risk of colorectal adenomas when compared with placebo (3953,3955,34612,34658). One clinical study shows that beta-carotene supplementation does not decrease the risk of adenoma recurrence in most patients with previous adenoma removal. Although it may decrease the risk of adenoma recurrence by 44% in patients who never smoke nor consume alcohol, it may actually increase the risk of adenoma recurrence by 107% in those patients who smoke and drink more than one alcoholic beverage daily (34500). Also, taking beta-carotene along with vitamin C, vitamin E, selenium, and calcium carbonate for 3 years does not reduce colorectal polyp growth when compared with placebo (12185,34676).

Lung cancer. Oral beta-carotene does not reduce the risk of lung cancer, and supplemental beta-carotene may actually increase lung cancer risk in some people.

^ Details: Taking beta-carotene 20-30 mg daily seems to increase the risk of lung cancer by 18% to 28% in people who smoke (especially those smoking more than 20 cigarettes per day), former smokers, people exposed to asbestos, and those who ingest significant amounts of alcohol (one or more drinks per day) in addition to smoking

(139,1471,2582,2642,3949,11303,11786,34522,34663,109770). A meta-analysis of clinical research in various populations shows that taking beta-carotene supplements increases the risk of lung cancer mortality by 14%; smoking status was not specified in this analysis (109767). However, beta-carotene from food does not seem to have this adverse effect. In patients diagnosed with lung cancer, clinical evidence shows that taking a combination of beta-carotene, alpha-tocopherol, and selenium does not decrease lung cancer-related mortality when compared with placebo after 5.25 years of use (34539).

Prostate cancer. Oral beta-carotene supplementation does not reduce the risk of prostate cancer in most males, and may actually increase risk in some people.

^ Details: The majority of reliable evidence shows that beta-carotene does not decrease prostate cancer risk in most people (148,1473,2406,7895,12877,34612). A large study in healthy males shows that taking 50 mg of beta-carotene every other day for nearly 13 years has no overall protective effect. However, some subgroups may benefit, such as those with low beta-carotene levels, low lycopene levels, or high body mass index (1447,1473,12877,14124). Some research suggests that a combination of beta-carotene, vitamin C, vitamin E, selenium, and zinc might reduce the risk of prostate cancer in patients with normal PSA levels (14135). However, the benefit might be due to the other ingredients.

There is also some concern that beta-carotene supplements might actually increase the risk of prostate cancer in some people. A large-scale population study shows that taking a multivitamin more than 7 times per week and also taking a separate beta-carotene supplement increases the risk of developing advanced prostate cancer (15607). Similarly, a large-scale clinical trial shows that smokers who take a beta-carotene supplement 20 mg daily for 5-8 years have an increased risk of developing prostate cancer (3959).

## INSUFFICIENT RELIABLE EVIDENCE to RATE

Age-related macular degeneration (AMD). Oral beta-carotene has only been evaluated in combination with other ingredients; its effect when used alone is unclear.

^ Details: Clinical research shows that taking an antioxidant combination including beta-carotene 15 mg, vitamin C 500 mg, vitamin E 400 IU, and zinc 80 mg daily reduces the odds of progression to advanced AMD by up to 31%. In patients with more severe AMD, this combination reduces the odds of progression to advanced AMD by 34%. This combination also reduces the odds of visual acuity loss by up to 29% in patients with severe AMD (7303,11326,90069). Evidence for the use of beta-carotene in low-risk patients with AMD is conflicting (6583,6584,7303).

There is contradictory evidence about the role of dietary beta-carotene for reducing the risk of developing AMD. Some evidence suggests that increasing dietary intake of beta-carotene might decrease the risk of developing AMD by up to 43% (5922). Other evidence suggests that increasing dietary beta-carotene alone does not reduce the risk of AMD. Increasing beta-carotene consumption also does not seem to be associated with a lower risk of age-related maculopathy (14007,34564). However, consuming above average amounts of dietary beta-carotene along with other nutrients such as vitamin E, vitamin C, and zinc might reduce risk of AMD by up to 35% (14257).

Aging skin. It is unclear if oral beta-carotene is beneficial for improving wrinkles and skin elasticity.

△ Details: A small study in females over 50 years of age shows that taking beta-carotene 30 mg daily for 90 days improves facial wrinkles and some measures of skin elasticity when compared with baseline. However, a dose of 90 mg daily does not seem to be beneficial (91381). The validity of this finding is limited by the lack of a comparator group.

Amyotrophic lateral sclerosis (ALS, Lou Gehrig's disease). It is unclear if oral beta-carotene is beneficial for improving symptoms of ALS.

^ Details: One large observational cohort study has found that supplemental beta-carotene 20 mg daily is not associated with reduced risk of ALS (90087). However, a meta-analysis of 5 observational cohort studies has found that the highest dietary intake of beta-carotene is associated with a 15% reduced risk of ALS when compared with the lowest intakes (90412).

Anxiety. It is unclear if oral beta-carotene is beneficial for preventing or treating anxiety.

^ Details: One observational study of middle-aged females has found that higher dietary intake of beta-carotene is associated with lower odds of anxiety during perimenopause, but not prior to menopause. Perimenopausal individuals with the highest dietary intake of beta-carotene had a 29% reduction in the odds of anxiety when compared with the lowest intakes (107288).

Asthma. It is unclear if oral beta-carotene is beneficial for asthma prevention.

^ Details: Observational research has found that dietary beta-carotene is not associated with a reduced incidence of asthma in children or adults (34567,107291). However, other observational research has found that a higher dietary intake of beta-carotene is associated with up to 33% lower odds of having asthma when compared with a lower dietary intake (109765). The effects of supplemental beta-carotene are unclear.

Chronic obstructive pulmonary disease (COPD). It is unclear if oral beta-carotene is beneficial for improving COPD.

Details: The prevalence of bronchitis and dyspnea in male smokers with COPD seems to be lower in those patients who consume a diet containing high amounts of beta-carotene (2580). However, taking beta-carotene supplements does not seem to

help (2580).

Cognitive function. It is unclear if oral beta-carotene is beneficial for improving cognitive function and memory.

^ Details: Observational research has found that consuming more beta-carotene in the diet over 22 years is associated with lower odds of poor cognitive function (104468). However, it is unclear if beta-carotene supplements are beneficial. Some clinical research shows that taking beta-carotene 50 mg on alternate days for 1 year does not improve cognitive performance, inclurer verbal memory, when compared with placebo in older males, long-term treatment of up to 18 years shows improvement in outcomes (34558).

Coronary heart disease (CHD). It is unclear if oral beta-carotene is beneficial for CHD.

^ Details: A meta-analysis of several population studies suggests that beta-carotene is associated with an 18% reduced risk of CHD per 5000 mcg/day of increased dietary intake and a 20% reduction in risk of CHD per 25 mcg/dL increase in beta-carotene blood concentration (109779).

Depression. It is unclear if oral beta-carotene is beneficial for depression.

^ Details: A meta-analysis of observational research has found that dietary intake of beta-carotene is inversely associated with depression. The highest intake of beta-carotene was associated with a 37% reduced risk of depression when compared with the lowest. Also, intakes of beta-carotene were lower in individuals with depression (109743). The effect of beta-carotene supplementation is unclear.

Exercise-induced asthma. It is unclear if oral beta-carotene is beneficial for improving exercise-induced asthma symptoms.

Details: A small clinical study in adults with exercise-induced asthma shows that taking a mixture of beta-carotene isomers 64 mg daily for 1 week seems to prevent asthma symptoms after 7 minutes of exercise (1474).

Fractures. It is unclear if oral beta-carotene is beneficial for fracture prevention.

^ Details: Observational research has found that increased beta-carotene consumption in the diet is associated with a lower fracture risk. Geographically, the reduced risk seems to be most prevalent in China and Singapore, while the risk reduction was not significant in the US and Europe (104466).

Gastric cancer. It is unclear if oral beta-carotene is beneficial for gastric cancer prevention.

^ Details: Preliminary clinical research in patients at risk for gastric cancer shows that taking beta-carotene orally 30 mg daily might increase regression of precancerous gastric lesions when compared with placebo (2579). It is unclear if this translates to decreased gastric cancer risk. In a meta-analysis of low-quality clinical research, beta-carotene did not decrease risk of gastric cancer when compared with placebo (12185). Beta-carotene in combination with vitamins A, C, and E also did not reduce gastric cancer risk (12185,34545). However, in a population of high-risk, malnourished Chinese adults, taking beta-carotene 15 mg daily plus vitamin E and selenium was associated with a decrease in gastric cancer incidence, but not mortality, when compared with placebo (2658,12185).

Hearing loss. It is unclear if oral beta-carotene is beneficial for hearing loss.

^ Details: Population research suggests that the highest dietary intake of beta-carotene is associated with a 12% decreased risk of developing self-reported hearing loss over a 22-year follow up period when compared with the lowest dietary intake (109807). Additionally, a small study in patients with idiopathic sudden sensorineural hearing loss shows that taking beta-carotene 26000 IU, ascorbic acid 200 mg, d-alpha-tocopherol 200 IU, and selenium 50 mcg twice daily for 30 days in addition to standard treatment improves hearing to a greater degree than standard treatment alone (101700).

Helicobacter pylori. It is unclear if oral beta-carotene is beneficial for Helicobacter pylori eradication.

^ Details: A small clinical study shows that taking beta-carotene 120 mg daily for 14 days, in combination with conventional Helicobacter pylori eradication therapy, does not improve the rate of eradication when compared with conventional eradication therapy alone (34472).

HIV/AIDS. It is unclear if oral beta-carotene is beneficial for HIV outcomes.

^ Details: A small clinical study in HIV-positive patients shows that taking beta-carotene 180 mg daily for one month increases total white blood cell count, CD4 cell counts, and CD4/CD8 ratios when compared with placebo (34667). However, taking the same dose of beta-carotene for a longer duration of 3 months does not improve these outcomes when compared with placebo in HIV-infected patients (34671).

Infant development. It is unclear if oral beta-carotene is beneficial for improving infant motor development.

^ Details: Observational research has found that a higher level of beta-carotene in breastmilk is associated with improved infant motor development when compared with lower levels (102157).

Influenza. Beta-carotene has only been evaluated in combination with other ingredients; its effect when used alone is unclear. Details: A large clinical trial in healthy Japanese adults shows that drinking 200 mL of a beverage containing beta-carotene 7.4-12.4 mg and Levilactobacillus brevis KB290 10 billion colony forming units daily for 12 weeks during influenza season does not reduce the risk of influenza or fever when compared with placebo. However, in a subgroup analysis of patients under 40 years of age, the risk of influenza was reduced by around 53% when compared with placebo (107287). It is unclear if these findings are due to beta-carotene, Levilactobacillus brevis, or the combination.

Irritable bowel syndrome (IBS). It is unclear if oral beta-carotene is beneficial for IBS.

^ Details: A small clinical trial in healthy adults with minor diarrhea-predominant IBS-like symptoms shows that taking a combination of beta-carotene 4.0-4.5 mg and Levilactobacillus brevis daily for 12 weeks modestly reduces abdominal pain and stool frequency when compared with placebo. There were no differences between groups in improvements in stool consistency, incomplete evacuation, or other symptoms (110960). Although this study included adults with diarrhea-predominant IBS-like symptoms, patients with diagnosed IBS were excluded, limiting the generalizability of the study.

Nonalcoholic fatty liver disease (NAFLD). It is unclear if oral beta-carotene might help prevent NAFLD.

Details: Observational research has found that higher intake and blood levels of beta-carotene are associated with 25% to 37% lower odds of NAFLD (101696).

Oral leukoplakia. Evidence for the use of beta-carotene for oral leukoplakia is conflicting.

^ Details: Some clinical research in patients with tobacco and/or betel nut chewing habits shows that taking beta-carotene 360 mg daily for 12 months induces complete remission in 33% of patients with oral leukoplakia, compared with 10% of patients receiving placebo (34674). A small clinical study shows that taking beta-carotene (Solatene, Hoffmann-LaRoche Inc.) 30 mg twice daily for 6 months induces remission in 52% of patients with oral leukoplakia when compared with baseline (1472). However, a lower dose of beta-carotene in combination with vitamin C did not seem to be beneficial. A small clinical study in Japanese non-

smoking adults with oral leukoplakia shows that taking beta-carotene 10 mg daily plus vitamin C 500 mg daily for 12 months does not improve clinical response or reduce the development of oral cancer over 5 years when compared with placebo (91384).

Oral mucositis. It is unclear if oral beta-carotene is beneficial for improving oral mucositis after radiation therapy.

Details: A small clinical study shows that taking beta-carotene 250 mg daily for up to 21 days followed by 75 mg daily for the remainder of radiation therapy or chemotherapy does not prevent the development of oral mucositis when compared with placebo (34637).

Osteoarthritis. It is unclear if oral beta-carotene is beneficial for reducing osteoarthritis progression.

△ Details: Observational research has found that higher dietary intake of beta-carotene is not associated with a reduced risk of developing osteoarthritis. However, the highest intake of beta-carotene is associated with a reduced rate of knee osteoarthritis progression when compared with lowest intake (5881).

Osteoporosis. It is unclear if oral beta-carotene is beneficial for reducing the risk of osteoporosis.

^ Details: Although observational studies in individuals 50 years of age and older has found that those with the highest dietary intake of beta-carotene had a 67% reduced odds of osteoporosis when compared with the lowest intake (107289), a meta-analysis of observational research shows that beta-carotene intake, based on dietary intake and serum levels, is not associated with risk of osteoporosis (109771). However, the highest intake of beta-carotene was associated with a 30% reduced risk of fractures in male, female, and Asian subgroups when compared with the lowest intake. Also, there was evidence of a small association between increased beta-carotene intake and increased overall bone density in Asian individuals, but not in individuals from studies published in the US, Europe, or Australia (109771).

Ovarian cancer. It is unclear if oral beta-carotene is beneficial for ovarian cancer prevention.

▲ Details: Observational research has found that a diet rich in carotenoids, including beta-carotene and especially alphacarotene, is associated with a lower risk of ovarian cancer in postmenopausal patients (10133).

Pancreatic cancer. It is unclear if oral beta-carotene is beneficial for pancreatic cancer prevention.

△ Details: A meta-analysis of low quality research shows that taking beta-carotene supplements, alone or in combination with other antioxidants such as vitamin A or vitamin E, does not reduce the risk of pancreatic cancer when compared with control (12185).

Parkinson disease. It is unclear if oral beta-carotene prevents Parkinson disease development.

△ Details: Observational research has found that beta-carotene intake is not associated with Parkinson disease risk (91164).

Physical performance. It is unclear if oral beta-carotene is beneficial for improving physical performance and muscle strength in older people.

△ Details: Population research has found that higher intake of dietary beta-carotene is associated with improved physical performance and muscle strength in elderly people (14006).

Polymorphous light eruption (PMLE). It is unclear if oral beta-carotene is beneficial for improving PMLE.

^ Details: Some small clinical studies show that taking beta-carotene orally 25-250 mg daily improves sun exposure tolerance when compared with baseline in patients with PMLE (34455,34652). However, one larger clinical study shows that beta-carotene 15-180 mg daily does not improve photosensitivity when compared with baseline (34673). The validity of the findings from each of these studies is limited by the lack of a comparator group.

Pre-eclampsia. It is unclear if oral beta-carotene is beneficial for pre-eclampsia prevention.

^ Details: Some epidemiological research has found that the highest intake of beta-carotene during pregnancy is associated with 69% reduced odds of having pre-eclampsia when compared with the lowest intake (109762). The effects of beta-carotene supplementation are unclear.

More evidence is needed to rate beta-carotene for these uses.

## **Dosing & Administration**

## Adult

Oral:

The Institute of Medicine has reviewed beta-carotene, but has not made recommendations for daily intake, citing lack of sufficient evidence. Consuming five servings of fruits and vegetables daily provides 6-8 mg of beta-carotene. Routine use of beta-carotene supplements is not necessary in the general population (4844).

See Effectiveness section for condition-specific information.

Certain dietary ingredients might reduce levels of beta-carotene in the body. Excessive consumption of alcohol, as well as Olestra, a non-calorie fat-substitute, can decrease serum concentrations of beta-carotene (2392,10134).

## Children

Oral:

The Institute of Medicine has reviewed beta-carotene, but did not make recommendations for daily intake, citing lack of sufficient evidence. Consuming 5 servings of fruits and vegetables daily provides 6-8 mg of beta-carotene. Routine use of beta-carotene supplements is not necessary in the general population (4844).

See Effectiveness section for condition-specific information.

## Standardization & Formulation

Beta-carotene supplements are available in both oil matrix gelatin capsules and water-miscible forms; the water miscible form seems to produce a significantly higher plasma beta-carotene level than oil matrix gelatin capsules (10136).

A specific product containing extract of Dunaliella salina (Betatene) has been used in clinical research (6134,34496). This product has been manufactured by two different companies. Betatene manufactured by Betatene Ltd. contains betacarotene 25 mg standardized to contain all-trans beta-carotene 13.0 mg, 9-cis beta-carotene 10.5 mg, other cis-isomers of beta-carotene 0.3 mg, alpha-carotene 0.75 mg, cryptoxanthin 0.18 mg, zeaxanthin 0.15 mg, and lutein 0.12 mg (6134,34496). Betatene manufactured by Cognis Australia Pty. Ltd. contains beta-carotene 24 mg standardized to contain all-trans beta-carotene 15.8 mg, 9-cis beta-carotene 5.8 mg, other cis beta-carotene isomers 2.0 mg, alpha-carotene  $^{\prime}$  mg, cryptoxanthin 0.25 mg, zeaxanthin 0.12 mg, and lutein 0.12 mg.

## Interactions with Drugs

#### NIACIN

Interaction Rating = Minor Be watchful with this combination.

Severity = Mild • Occurrence = Possible • Level of Evidence = A

Beta-carotene might decrease the beneficial effects of niacin on high-density lipoprotein (HDL) cholesterol levels.

A combination of niacin and simvastatin (Zocor) effectively raises high-density lipoprotein (HDL) cholesterol levels in patients with coronary disease and low HDL levels. Clinical research shows that taking a combination of antioxidants (beta-carotene, vitamin C, vitamin E, and selenium) along with niacin and simvastatin attenuates this rise in HDL, specifically the HDL-2 and apolipoprotein A1 fractions, by more than 50% in patients with coronary disease (7388,11537). It is not known whether this adverse effect is due to a single antioxidant such as beta-carotene, or to the combination. It also is not known whether it will occur in other patient populations.

## ♠ Interactions with Supplements

LUTEIN: Beta-carotene supplements might decrease body stores of lutein.

▲ Details

Some clinical research shows that beta-carotene supplementation lowers serum lutein concentrations (10134).

#### ♠ Interactions with Conditions

## **ASBESTOS EXPOSURE**

Taking beta-carotene supplements appears to increase the risk of certain types of cancer, including lung and stomach cancer, in patients who have been exposed to asbestos (34591). Do not take beta-carotene supplements if you have been exposed to asbestos.

### **∧** SMOKERS

Taking beta-carotene supplements appears to increase the risk of cancer in smokers. Cigarette smoking decreases serum concentrations of beta-carotene and other carotenoids, and depletes body stores of beta-carotene (7722,10134). However, beta-carotene supplementation should not be recommended because supplemental beta-carotene in doses greater than 20 mg daily is associated with a significantly higher risk of recurrent colorectal adenomas, as well as lung and prostate cancer in smokers (139,3949,3959,6382,6393,34500). The increased risk seems to be especially applicable to those that started smoking at 21 years or older and those that smoke at least 21 cigarettes a day (104467). Tell smokers to avoid taking beta-carotene supplements.

## Interactions with Lab Tests

None known.

## ∧ Nutrient Depletion

## SOME DRUGS CAN AFFECT BETA-CAROTENE LEVELS:

# **BILE ACID SEQUESTRANTS**

Depletion Rating = Insignificant Depletion A supplement is not needed for most patients.

Bile acid sequestrants may modestly reduce absorption of beta-carotene.

▲ Details

Cholestyramine (Questran) and colestipol (Colestid) can reduce absorption of fat-soluble vitamins, including beta-carotene (4454,4457,4458,4461,5919). Serum levels of beta-carotene can be reduced (4457,4461), but this is probably only in proportion to the lowering of cholesterol (on which beta-carotene is transported). Supplements are not usually needed (4461).

### COLCHICINE

Depletion Rating = Insignificant Depletion A supplement is not needed for most patients.

Colchicine might modestly reduce absorption and levels of beta-carotene.

▲ Details

Limited evidence suggests that short-term treatment with colchicine 1.9-3.9 mg daily can reduce absorption and serum levels

of beta-carotene. Theoretically, this is due to disruption of intestinal mucosal function (4543). Long-term use of 1 to 2 mg daily does not affect beta-carotene levels (5921). Advise patients that this is unlikely to be clinically significant.

#### MINERAL OIL

Depletion Rating = Insignificant Depletion A supplement is not needed for most patients.

Mineral oil might modestly reduce absorption and levels of beta-carotene.

Mineral oil is a laxative and reduces absorption of fat-soluble vitamins, including beta-carotene (4454,4495,4496). This is not likely to be clinically significant when mineral oil is used for 4 months or less (4496).

#### NEOMYCIN

Depletion Rating = Insignificant Depletion A supplement is not needed for most patients.

Neomycin might modestly reduce levels of beta-carotene.

▲ Details

Oral neomycin sulfate in doses of 4-12 grams per day causes malabsorption and can reduce beta-carotene absorption. However, this is not likely to be clinically significant with short-term neomycin use (5916).

## ORLISTAT (Xenical, Alli)

Depletion Rating = Major Depletion A supplement is needed for most patients.

Orlistat can decrease absorption of beta-carotene and other fat-soluble vitamins.

▲ Details

Orlistat blocks the enzyme that breaks down fat for absorption. Theoretically, in addition to reducing fat absorption, it might also reduce absorption of fat-soluble vitamins like beta-carotene. Recommend that patients take a multivitamin supplement, and separate the dosing time by at least 2 hours from orlistat (6001).

## **PROTON PUMP INHIBITORS**

Depletion Rating = Insufficient Evidence to Rate Clinical significance is not known.

Proton pump inhibitors might reduce absorption of beta-carotene.

▲ Details

Proton pump inhibitors reduce stomach acid, which might in turn reduce absorption of supplemental beta-carotene (31), but it is not known if this is clinically significant, or if it affects absorption of dietary beta-carotene.

## SIMVASTATIN (Zocor)

Depletion Rating = Insignificant Depletion A supplement is not needed for most patients.

Simvastatin might modestly reduce levels of beta-carotene.

▲ Details

Clinical research shows that simvastatin can reduce serum levels of circulating beta-carotene (24554), but this is probably only in proportion to the lowering of cholesterol (on which beta-carotene is transported). Supplements are not usually needed (4461).

## Overdose

## Presentation

Although beta-carotene is partly metabolized to vitamin A, high intake of beta-carotene does not result in vitamin A toxicity because the proportion converted to vitamin A decreases as beta-carotene intake increases (8044). High oral doses of betacarotene in foods or supplements can cause yellow or orange skin pigmentation called carotenoderma (11786,34572,34594,91382).

### Treatment

There is insufficient reliable information available about the treatment of overdose with beta-carotene.

# **Commercial Products Containing: Beta-Carotene**

## View All

View Health Canada Licensed Products



View Certified Products





**USP Verified Products** 



**NSF Contents Certified Products** 



**NSF Certified for Sport Products** 

## **Pharmacokinetics**

Absorption: Absorption of beta-carotene is variable. The intestine has a limited capacity to absorb intact beta-carotene (8044). Beta-carotene appears to be absorbed better from supplements than food (34490). The amount of beta-carotene absorbed from food is only about 5% to 30% of that from synthetic supplements due to complexes it forms with proteins and fiber. Heating food may break down these complexes (2628). Beta-carotene requires some dietary fat for absorption, but supplemental beta-carotene is similarly absorbed when taken with high-fat (36 grams fat) or low-fat (3 grams fat) meals (2628,6133). The amount of beta-carotene absorbed and converted to vitamin A also depends upon the individual's vitamin A status, beta-carotene bod stores, and the amount of beta-carotene ingested (2628,8044). Age does not appear to play a role in the ability to absorb and beta-carotene (34509).

There is more than one isomer of beta-carotene and there may be differences in their absorption. The 9-cis-beta-carotene isomer is poorly absorbed, and most of it is converted to all-trans-beta-carotene in the intestine (2628).

Beta-carotene supplements are available in both oil matrix gelatin capsules and water-miscible forms. Some clinical trials have used water-miscible beta-carotene (10%) beadlets. The water miscible form seems to produce a 47% to 50% higher plasma beta-carotene level than oil matrix gelatin capsules (10136).

Metabolism: Some ingested beta-carotene is converted to vitamin A in the intestinal mucosa (2628,34660), while some is converted to vitamin A in the liver (34660). Although beta-carotene is partly metabolized to vitamin A, high intake of beta-carotene does not result in vitamin A toxicity because the proportion converted to vitamin A decreases as beta-carotene intake increases (8044). Age does not appear to play a role in the ability to convert beta-carotene to vitamin A (34509).

Distribution: The cis isomers of beta-carotene account for less than 5% of carotenoids in plasma, but 10% to 25% of carotenoids in the tissues are beta-carotene cis isomers (2628). Carotenoids are mainly carried in the blood on low-density lipoproteins (LDLs) (2628).

Excretion: Beta-carotene is excreted in the feces (91385). In a single male, the mean residence time for beta-carotene was 51 days (34660).

#### **Mechanism of Action**

**General**: Beta-carotene belongs to a class of red, orange, and yellow pigments called carotenoids. There are hundreds of varieties of provitamin A carotenoids, which are present in many fruits, grains, oils, and vegetables (2628,8044). Commercially available beta-carotene is produced synthetically or from palm oil, algae, or fungi (11786).

Beta carotene is converted to retinal, which is essential for vision and is subsequently converted to retinoic acid, which is used for processes involving growth and cell differentiation (7135,8044). The typical dietary intake of beta-carotene in American adults varies from 0.5 to 6.5 mg per day (2628). Beta-carotene is closely related to alpha-carotene; both are precursors for vitamin A (2628). Beta-carotene and other carotenoids provide approximately 50% of the vitamin A needed in the American diet (8044).

Beta-carotene consists of a number of isomers. Synthetic beta-carotene, the form used in most of the clinical studies, is composed of the all-trans form. Natural beta-carotene sources contain 9-cis-, 13-cis-, and 15-cis-beta-carotene (1474). The 9-cis-beta-carotene isomer is poorly absorbed, and most of it is converted to all-trans-beta-carotene in the intestine (2628). The cis isomers account for less than 5% of carotenoids in plasma, but 10-25% of carotenoids in the tissues are beta-carotene cis isomers (2628). Little is known about the pharmacology of beta-carotene and the differences that may exist between the various isomers and the natural and synthetic forms (2628). Beta-carotene has activity independent of its conversion to vitamin A (139,1470).

Anti-inflammatory effects: Serum beta-carotene levels seem to be inversely related to C-reactive protein levels and the white blood count. These markers are markers of inflammation and are associated with tumor recurrence and arteriosclerotic cardiovascular disease events (10135). In humans, beta-carotene decreases levels of tumor necrosis factor (TNF)-alpha (34487).

Antioxidant effects: Beta-carotene seems to have antioxidant activities and prevent lipid peroxidation (139,34487). It has been proposed that the antioxidant effects may help prevent cancer by reducing free radical-induced DNA damage (2592,2599). However, beta-carotene does not have antioxidant effects in all human or laboratory studies, suggesting dose, specific outcome measures, and/or and health of the individual may play a role (34464,34473).

Cancer effects: There seems to be an inverse relationship between dietary carotenoid intake, or serum beta-carotene levels, and the incidence of various cancers (1444,34551,34578,34609,34610,34611,34628,34634). In vitro studies show that beta-carotene and palm oil carotene inhibit tumor cell growth (2592,2628,14045). There is preliminary evidence that carotenoids, including beta-carotene, can inhibit breast cancer cell growth regardless of estrogen receptor status (8045). However, dietary beta-carotene is not substantially concentrated in breast adipose tissue. Breast adipose tissue concentrations are only slightly higher than serum concentrations (10243).

There is also evidence that the inhibitory effect on cancer cell growth by certain statin drugs with a closed ring structure, such as mevastatin and lovastatin (Mevacor), may be enhanced when used with carotenoids (8046). However, anticancer effects of betacarotene supplementation have not been effectively demonstrated in humans.

Despite these potential positive effects, there is some concern that beta-carotene metabolites with pharmacological activity can accumulate and have carcinogenic effects (6377,6393). Components of cigarette smoke can degrade beta-carotene, and lower concentrations of beta-carotene have been reported in both active and passive smokers (2592,2593). Smoking might enhance production of carcinogenic beta-carotene oxidation metabolites which, if not neutralized by other antioxidants (such as tocopherol and ascorbate, which are also often depleted in smokers), could lead to increased risk of lung cancer (2628,6377). In addition, beta-carotene metabolites might increase the binding of carcinogenic metabolites to DNA and inhibit gap-junction communication between normal cells and tumor cells. Beta-carotene itself might also increase the levels of certain cytochrome P450 (CYP450) dependent enzymes that can hydroxylate and activate certain compounds into their highly carcinogenic forms (6393), as well as increase catabolism of retinoic acid, which controls lung epithelial cell proliferation and differentiation (2592).

Cardiovascular effects: There is some evidence to suggest that dietary intake of beta-carotene from fruits and vegetables is associated with a reduced risk of cardiovascular disease (CVD) (34585). However, taking beta-carotene supplements does not appear to reduce CVD risk in general (1448,2646) and may increase risk, at least in smokers (2642,3937,3949).

**Dermatologic effects**: In humans, beta-carotene reduces signs of aging of the skin. Mechanisms of action may involve increproduction of collagen and reduced harmful ultraviolet-induced oxidative or other reactions in the skin (91381).

## Classifications

Carotenoids

## References

See Monograph References

Monographs are reviewed on a regular schedule. See our Editorial Principles and Process for details. The literature evaluated in this monograph is current through 12/7/2023. This monograph was last modified on 4/30/2024. If you have comments or suggestions, please tell the editors.

© 2024 Therapeutic Research Center. Commercial distribution or reproduction prohibited

Privacy Policy | Terms of Use | Technical Support | Site Map | Contact Us