

A Pharmacist's Guide to the Safe Use of Niacin for the Treatment of Dyslipidemias



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Niacin is a water-soluble B complex vitamin that helps convert food into energy and is essential for promoting the health of the skin, blood cells, brain, and nervous system. The recommended daily allowance is 16 mg for men and 14 mg for women.

Niacin also is the oldest known lipid-modifying agent still in use. When administered in doses well above the recommended daily allowance—usually 1.5 g to 3 g daily—niacin lowers levels of low-density lipoprotein (LDL) cholesterol by about 5% to 25%, and lowers triglyceride levels by about 20% to 35%. Niacin also raises high-density lipoprotein (HDL) cholesterol levels more than any other lipid-modifying therapy, generally by 15% to 35% (although increases of 40% have been seen with very high doses).

Because niacin can be used as both a nutritional supplement and a treatment for dyslipidemias, product selection has an important impact on clinical outcomes. Critical factors in careful product selection include active ingredient, regulatory status, and formulation.

Nicotinic Acid vs Nicotinamide

Vitamin B₃ has two principal components: nicotinic acid and its amide, nicotinamide. The term “niacin” usually is meant to refer specifically to nicotinic acid; accordingly, nicotinic acid and nicotinamide also are known as niacin and niacinamide. However, “niacin” sometimes is used as a collective term to refer to both nicotinic acid and nicotinamide.

Niacin products used for lipid-modifying therapy should contain nicotinic acid only. Although nicotinic acid and nicotinamide have identical vitamin activities, they have very different pharmacologic activities. Nicotinamide has no effect on lipid levels

Reviewed by:

Ralph E. Small, PharmD, Professor Emeritus, Virginia Commonwealth University.

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and cannot be used in place of nicotinic acid to treat dyslipidemias.

Flushing of the face and trunk is a common and bothersome adverse effect of niacin therapy. Niacin products that are promoted as being “no flush” or “flush free” often contain inositol hexaniacinate, a compound consisting of six molecules of nicotinic acid esterified to one inositol molecule. In theory, this compound is associated with little or no flushing because of its slow hydrolysis to free nicotinic acid and inositol. In reality, the absence of flushing may reflect an absence of active ingredient. None of the 10 no-flush niacin preparations tested in one study produced detectable free nicotinic acid.¹

Prescription Drugs vs Dietary Supplements

Some products containing niacin are available by prescription only. Others are available directly to consumers as dietary supplements. The American Heart Association (AHA) warns that dietary supplement niacin must *not* be used as a substitute for prescription niacin and should not be used for cholesterol-lowering because of potentially serious adverse effects.

This warning stems in part from the fact that dietary supplements are not required to be approved by the Food and Drug Administration before they are marketed. Each manufacturer is responsible for ensuring that its dietary supplement products are safe and that the content matches the amount declared on the label; there currently are no good manufacturing practice regulations. As a result, dietary supplement niacin may contain widely variable amounts of niacin—from none to much more than the label states. The amount of niacin may even vary from lot to lot of the same brand.

Immediate- vs Extended- vs Sustained-Release Formulations

The AHA warning also reflects problems with sustained-release formulations of niacin. Niacin is available in three formulations:

- Immediate-release (also called “crystalline” or “plain” niacin).
- Sustained-release (also marketed as “long-acting,” “controlled-release,” or “timed-release” niacin).
- Extended-release.

Immediate-release niacin is available both as a prescription drug (Niacor, Upsher-Smith) and as dietary supplement products. Sustained-release niacin is available as dietary supplement products only. Extended-release niacin is available as a prescription drug only (Niaspan, Kos Pharmaceuticals).

The sustained-release preparations were developed in an effort to limit niacin-induced flushing. They did; unfortunately, they also proved to be more hepatotoxic than immediate-release niacin, especially if the absorption period exceeded 12 hours or if the dosage exceeded 2 g/day. Notably, cases of severe hepatic toxicity, including fulminant hepatic necrosis, have occurred when sustained-release niacin products were substituted for immediate-release niacin at equivalent doses.

The pharmacokinetic profile of extended-release niacin falls between those of immediate-release and sustained-release formulations. This intermediate release minimizes both the flushing associated with immediate-release niacin and the hepatotoxicity seen with sustained-release preparations.

The Bottom Line

Prescription immediate-release or extended-release niacin should be used whenever possible for the treatment of dyslipidemias. Immediate-release and extended-release products have similar efficacy, but they should not be used interchangeably. Pharmacists should discourage patients from attempting to self-treat dyslipidemias with dietary supplement niacin.

¹Meyers CD, Carr MC, Park S, et al. Varying cost and free nicotinic acid content in over-the-counter niacin preparations for dyslipidemia. *Ann Intern Med.* 2003;139:996-1002.

A Patient's Guide to the Safe Use of Niacin for High Cholesterol



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Vitamins are substances that your body needs in very small amounts to help it function properly. Niacin (NYE-a-sin), also called vitamin B₃, helps convert food into energy. It also helps to keep your skin, blood cells, brain, and nervous system healthy.

People who don't get enough niacin can develop a condition called pellagra, which causes scaly skin sores, inflamed mucous membranes, diarrhea, and mental confusion and delusions. Pellagra is very rare today, because many of the foods we eat have added niacin. But people who do develop pellagra may need to take niacin supplements. These supplements are available without a prescription.

Niacin also is used to treat high cholesterol. Niacin lowers the levels of "bad" cholesterol (low-density lipoprotein, or LDL, cholesterol) and triglycerides in the blood. It also raises the levels of "good" cholesterol (high-density lipoprotein, or HDL, cholesterol). The niacin products approved for treating high cholesterol are available only with a doctor's prescription.

If you have high cholesterol, you may be tempted to buy some niacin supplements and take them on your own, or use the supplements instead of prescription niacin. But in the case of niacin, what you don't know *can* hurt you. The American Heart Association warns that niacin supplements must *not* be used as a substitute for prescription niacin. They also should *not* be used for lowering cholesterol because of potential very serious side effects.

Supplements vs Prescription Niacin

Niacin supplements are not regulated by the Food and Drug Administration (FDA) the same way that prescription niacin is. Prescription products undergo extensive review before they are approved for marketing. The manufacturer must provide evidence that the product is both safe and effective for its intended

use. The manufacturer also must follow "good manufacturing practices," which are meant to ensure that the product contains the stated ingredient in the stated amount.

In contrast, dietary supplements are not reviewed by the FDA before they are marketed. Each manufacturer is responsible for ensuring that its products are safe and that the content matches the amount declared on the label; there currently are no good manufacturing practice regulations. Because of this relative lack of oversight, niacin supplements may contain widely variable amounts of niacin—from none to much more than the label states. The amount of niacin may even vary from batch to batch of the same brand.

Niacin supplements also may not contain the right active ingredient for treating high cholesterol. The term "niacin" may be used to refer to two components of vitamin B₃: nicotinic acid and a related compound, nicotinamide (also called niacinamide). Only nicotinic acid has an effect on cholesterol levels. Niacin supplements may contain both nicotinic acid and nicotinamide, and therefore not be as effective as prescription niacin. Or they may contain just nicotinamide, and therefore not be effective at all.

Because niacin supplements are not approved for treating high cholesterol, their labels do not contain information about proper dosage, possible side effects, and other important information. The dosage of niacin used to treat cholesterol is much higher than the dosage used for vitamin deficiencies. If you try to take niacin on your own—without your doctor's supervision—you may take an ineffective dosage, or even a dangerous dosage. Or you may experience troublesome side effects that could be managed easily if you had the right information.

Niacin Formulations

Niacin is available in three formulations:

- Immediate-release niacin (also called "crystalline" or "plain" niacin).
- Sustained-release niacin (also marketed as "long-acting," "controlled-release," or "timed-release" niacin).
- Extended-release niacin.

Immediate-release niacin is available both by prescription (the brand name is Niacor) and as a supplement. Sustained-release niacin is available as a supplement only. Extended-release niacin is available by prescription only (the brand name is Niaspan).

The sustained-release preparations were developed in an effort to reduce some of the troublesome side effects of immediate-release niacin, especially skin flushing and itching. The sustained-release preparations did reduce those side effects, but unfortunately, they also caused liver problems. The most serious problems occurred when people stopped using immediate-release niacin and began using the same dose of sustained-release niacin.

Extended-release niacin falls somewhere in between immediate-release and sustained-release niacin. It reduces the troublesome side effects of immediate-release niacin without causing the liver problems seen with sustained-release niacin.

The Bottom Line

If you have high cholesterol, don't attempt to treat it on your own, especially with niacin supplements. Ask your doctor if you are a candidate for a prescription niacin product.

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