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# Vitamin B3

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## Indications

Niacin, known as vitamin B3, is a water-soluble, vitamin of the B complex group of vitamins. Food such as bran, yeast, eggs, peanuts, poultry, red meat, fish, whole-grain cereals, legumes, and seeds are rich sources of the vitamin. As a drug, it is used for 2 main indications:

1. Deficiency of the vitamin, also known as pellagra
2. Dyslipidemia

### Indication for Pellagra

Pellagra is the deficiency of vitamin B3. Niacin is indicated in the treatment of pellagra until the symptoms resolve, most commonly for the relief of skin symptoms.

### Indication for Dyslipidemia

Therapeutic doses of niacin can reduce the level of total cholesterol up to 25%, low-density lipoprotein (LDL) up to 10% to 15%, and triglycerides by up to 20% to 50%. Niacin has the highest efficacy to raise high-density cholesterol (HDL), with an increase of 15% to 35%.[1] It is used in moderate to high doses (1000 to 3000 mg per day) for refractory dyslipidemia and cases warranting HDL increase.

With more evaluation, niacin may be grouped with hypolipidemic drugs used for patients with[2]:

- Concomitant hypercholesterolemia and statin intolerance
- Metabolic syndrome
- Patients unresponsive to hypolipidemic therapy of targeted LDL cholesterol values

## Mechanism of Action

Niacin is needed for adequate cellular metabolism and function as a vital component in coenzyme 1 (the oxidized form of nicotinamide adenine dinucleotide [NAD]) and coenzyme 2 (the reduced form of nicotinamide adenine dinucleotide phosphate [NADP]), which either accept or donate hydrogen ions in essential oxidation-reduction reactions. They are important coenzymes for glycolysis, pyruvate metabolism, protein, and amino acid metabolism, pentose biosynthesis, glycerol metabolism, synthesis of high energy phosphate bonds, and fatty acid metabolism.[3] As cellular functions in many organs and tissues are affected by the deficiency of niacin, the clinical expression of pellagra is diverse.

Mechanism of action of niacin in dyslipidemia includes inhibition of lipolysis within adipose tissue, reduction in liver triacylglycerol formation, increase in lipoprotein lipase activity, inhibition of synthesis of apo B-100 and hepatic very low-density lipoprotein (VLDL), impaired cholesterol biosynthesis and lowering of the fractional catabolic rate of HDL-Apo A-1. Apo A-1, which is an activator of lecithin cholesterol acyltransferase (LCAT), has a major role in reverse cholesterol transport.[4]

Niacin decreases the risk of cardiovascular disease by exhibiting a plethora of pleiotropic effects, especially by its anti-oxidative and anti-inflammatory actions and by increasing serum adiponectin.[2]

## Administration

Recommended daily allowance of niacin is as follows:[5]

- Infants: 5 to 6 mg
- Children: 9 to 13 mg
- Adults: 13 to 20 mg
- Pregnant and lactating mothers: 17 mg and 20 mg, respectively

### Dosing

#### *Pellagra*

The adult dose is nicotinamide 100 mg orally, every 6 hours for several days until relief of acute symptoms, followed by 50 mg 8 to 12 hourly until all skin lesions heal. In severe cases (marked neurological or gastrointestinal tract symptoms), 1 g 3 to 4 times a day can be given, initially by the parenteral route. For children, one can use 10 to 50 mg orally every 6 hours until symptoms of pellagra resolve. For mild endemic pellagra, smaller doses such as 10 mg per day can be used. Therapy should include other B vitamins, magnesium, and zinc as well as a calorie-rich diet. Topical emollients may reduce discomfort due to skin lesions.[3] Sustained-release (SR) formulations have been developed which are available over-the-counter. Sustained-release niacin can be administered once daily and is less likely to cause flushing. However, it is not approved for use in hyperlipidemia, and some studies showed a high likelihood of hepatotoxicity.

#### *Dyslipidemia*

The recommended dose for hyperlipidemia is 1 to 6 g daily, initially low doses (100 mg three times per day), increasing at weekly intervals depending upon effect and tolerance. Extended-release (ER) niacin in concentrations from 125 to 1000 mg is approved for use in hyperlipidemia and does not have hepatotoxicity compared to regular niacin.[6]

## Adverse Effects

#### *Flushing*

Niacin causes vasodilation of small subcutaneous blood vessels mediated by prostaglandin D2 that leads to a cutaneous flush, accompanied by an uneasy sensation of pruritus and warmth. Severe flushing may lead to hypotension and dizziness. Flushing appears earlier after dosing with immediate-release (IR) niacin (approximately 30 minutes) and delayed for sustained-release niacin (2 to 4 hours). Patients should avoid hot showers immediately after a dose, and if necessary, aspirin or ibuprofen is helpful.

#### *Peptic Ulcer Disease*

Niacin therapy may aggravate peptic ulcer disease. Niacin should be used cautiously with active or chronic gastrointestinal disorders.

***Hepatotoxicity***

The most serious adverse effect is niacin hepatotoxicity. Mild increase in hepatic transaminase levels up to twice the upper limit of the normal range is common.

***Hyperglycemia***

Decreased glucose tolerance and hyperglycemia can occur in individuals with diabetes and is thought to result from insulin resistance consequent to the free fatty acid rebound after moderately-sized doses.

***Arrhythmia***

Patients with supraventricular tachycardias (SVTs) may experience unusual chest sensations and palpitations even when the SVTs are controlled via concomitant antiarrhythmic therapy.

***Eye Symptoms***

Retinal edema or toxic amblyopia resulting in blurred vision is also reported.[7]

***Pellagra***

Vitamin B3 underdosing in vulnerable population groups may result in pellagra, which is characterized by 4 Ds in clinical manifestations: diarrhea, dermatitis, dementia, and death.

*Dermatitis:* The diagnosis is challenging in the absence of the skin lesions and is more easily made if characteristic skin lesions are present. Dermatitis begins as erythema, resembles sunburn in the initial stages, but tanning occurs more slowly than typically seen in sunburn. The lesion is a bilaterally symmetrical eruption located at sites of sunlight exposure.[8] Cutaneous patches on the neck are known as Casal necklace. It extends as a broad collar around the cervical dermatomes C3 and C4 in the neck.

*Diarrhea:* Gastrointestinal disturbances include diarrhea, nausea, vomiting, epigastric discomfort, poor appetite, abdominal pain, and increased salivation. Stools are typically watery but can be bloody or mucoid occasionally.

*Neurologic manifestation:* Presents as nonspecific symptoms like confusion, hallucinations, irritability, psychomotor unrest, ataxia, and depression. As the disease advances, patients become confused, disoriented and delirious, then comatose and stuporous, and finally die.

## Contraindications

Contraindications to the use of niacin are as follows:

- Peptic ulcer disease
- Active hepatic disease or elevation in transaminases
- Hypersensitivity reactions

## Monitoring

### Niacin Therapy for Pellagra

A combined excretion of pyridone and N-methylnicotinamide of less than 1.5 mg in 24 hours points toward severe niacin deficiency.

### Niacin therapy for Dyslipidemia

Monitoring of uric acid, blood glucose, and potassium is recommended.[9]

***Maximum Tolerated Dose of Niacin***

*Immediate-Release formulation:* 6 g/day in 2 to 3 divided doses

*Sustained-Release formulation:* 2000 mg per day[6]

## Toxicity

Symptoms of toxicity include nausea, vomiting, diarrhea, flushing, dizziness, and palpitations. Treatment of toxicity involves supportive care including gastric lavage.

## Questions

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## References


1. Isaac S. The "gauntlet" of pellagra. Int. J. Dermatol. 1998 Aug;37(8):599. [PubMed: 9732006]
2. Park YK, Sempos CT, Barton CN, Vanderveen JE, Yetley EA. Effectiveness of food fortification in the United States: the case of pellagra. Am J Public Health. 2000 May;90(5):727-38. [PMC free article: PMC1446222] [PubMed: 10800421]
3. Pownall HJ, Jackson RL, Roth RI, Gotto AM, Patsch JR, Kummerow FA. Influence of an atherogenic diet on the structure of swine low density lipoproteins. J. Lipid Res. 1980 Nov;21(8):1108-15. [PubMed: 7462806]
4. Hegyi J, Schwartz RA, Hegyi V. Pellagra: dermatitis, dementia, and diarrhea. Int. J. Dermatol. 2004 Jan;43(1):1-5. [PubMed: 14693013]
5. Kashyap ML. Mechanistic studies of high-density lipoproteins. Am. J. Cardiol. 1998 Dec 17;82(12A):42U-48U; discussion 85U-86U. [PubMed: 9915662]
6. Kashyap ML, McGovern ME, Berra K, Guyton JR, Kwiterovich PO, Harper WL, Toth PD, Favrot LK, Kerzner B, Nash SD, Bays HE, Simmons PD. Long-term safety and efficacy of a once-daily niacin/lovastatin formulation for patients with dyslipidemia. Am. J. Cardiol. 2002 Mar 15;89(6):672-8. [PubMed: 11897208]
7. McKenney JM, Proctor JD, Harris S, Chinchili VM. A comparison of the efficacy and toxic effects of sustained- vs immediate-release niacin in hypercholesterolemic patients. JAMA. 1994 Mar 02;271(9):672-7. [PubMed: 8309029]
8. Schwartz ML. Severe reversible hyperglycemia as a consequence of niacin therapy. Arch. Intern. Med. 1993 Sep 13;153(17):2050-2. [PubMed: 8357290]
9. Zeman M, Vecka M, Perlík F, Hromádka R, Staňková B, Tvrzická E, Žák A. Niacin in the Treatment of Hyperlipidemias in Light of New Clinical Trials: Has Niacin Lost its Place? Med. Sci. Monit. 2015 Jul 25;21:2156-62. [PMC free article: PMC4523006] [PubMed: 26210594]





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