

Therapeutic Class Overview Niacin Derivatives

Therapeutic Class

- Overview/Summary:** Niacin favorably affects all lipids and lipoproteins when given in pharmacological doses; however, the mechanism of action is not completely understood.¹⁻⁵ Niacin has several effects on lipid metabolism including inhibition of hepatic production of very low-density lipoprotein cholesterol, and consequently its metabolite low-density lipoprotein cholesterol. In addition, it decreases plasma concentrations of triglycerides (20 to 50%), very low-density lipoprotein remnants, and intermediate density lipoprotein. Administration of niacin also causes a shift in low-density lipoprotein composition from small, dense particles to larger, more buoyant particles. Lastly, niacin increases high density lipoprotein cholesterol (15 to 35%) both by reducing lipid transfer of cholesterol from high density lipoprotein cholesterol to very low-density lipoprotein cholesterol, and by delaying high density lipoprotein cholesterol clearance. Niacin can decrease low-density lipoprotein cholesterol by 5 to 25%.¹⁻⁵

There are over-the-counter niacin products that are currently available, and these products are labeled as dietary supplements. While these supplements are “generally recognized as safe”, the Food and Drug Administration (FDA) does not examine the efficacy and safety of these products or regulate the manufacturing process. The FDA has imposed statutory restrictions prohibiting manufacturers of dietary supplements from claiming that their products “treat, cure, or prevent any disease”. Without FDA regulation, the content of nicotinic acid in niacin products is not guaranteed.⁶

Table 1. Medications Included Within the Therapeutic Class Review⁴⁻¹²

Generic (Trade Name)	Food and Drug Administration Approved Indications	Dosage Form/Strength	Generic Availability
Niacin (Niacor [®] , Niaspan [®])	Hypertriglyceridemia, adjunctive therapy for the treatment of adult patients with severe hypertriglyceridemia who present a risk of pancreatitis and who do not respond adequately to a determined dietary effort to control them; Primary hypercholesterolemia and mixed dyslipidemia, adjunct to diet, alone or in combination with a bile acid binding resin, for reduction of elevated total cholesterol (TC) and low-density lipoprotein cholesterol (LDL-C) in patients with primary hypercholesterolemia, adjunct to diet and in combination with a bile acid binding resin to reduce elevated TC and LDL-C levels in adult patients with primary hyperlipidemia and adjunct to diet to reduce elevated TC, LDL-C, apolipoprotein B, and TG levels, and to increase high-density lipoprotein cholesterol in patients with primary hyperlipidemia and mixed dyslipidemia; Secondary prevention of cardiovascular disease, adjunct to diet to reduce the risk of recurrent nonfatal myocardial infarction in patients with a history of myocardial infarction and hyperlipidemia and adjunct to diet and in combination with a bile acid binding resin to slow progression or promote regression of atherosclerotic disease in patients with a history of coronary artery disease and hyperlipidemia	Extended-release tablet (Niaspan [®]):* 500 mg 750 mg 1,000 mg Tablet (Niacor [®]):* 500 mg	✓

*Generic is available in at least one dosage form or strength.

Evidence-based Medicine

- Clinical trials have demonstrated the safety and efficacy of the niacin derivatives.⁷⁻³⁹
- In a trial comparing niacin extended-release and immediate-release formulations, doses $\geq 1,500$ mg/day of niacin extended-release decreased low-density lipoprotein cholesterol to a significantly greater extent ($P < 0.04$ or $P < 0.01$); however, at all doses niacin immediate-release significantly increased high-density lipoprotein cholesterol ($P < 0.04$ or $P < 0.01$). Reductions in triglycerides were similar between the two formulations, except for niacin immediate-release 1,000 mg/day which led to significantly greater reductions ($P = 0.009$).²²
- Direct comparisons of niacin with other lipid modifying agents demonstrated that no one medication class is consistently more efficacious over another in achieving significant alterations in individual lipid parameters, and results support the use of the niacin as combination therapy with other lipid modifying agents.⁷⁻³⁹

Key Points within the Medication Class

- According to Current Clinical Guidelines:⁴⁰⁻⁴⁸
 - In general, therapeutic lifestyle changes, including diet, exercise and smoking cessation, remain an essential modality in the management of patients with hypercholesterolemia.
 - When low-density lipoprotein cholesterol (LDL-C) lowering is required, initial treatment with a statin, a bile acid sequestrant or niacin is recommended. However, in general, the statins are considered first line therapy for decreasing LDL-C levels, and are recommended in patients with established coronary heart disease or coronary heart disease equivalents.
 - In patients with an elevated triglyceride level (≥ 500 mg/dL) a fibric acid derivative or niacin should be initiated before LDL-C lowering therapy to prevent pancreatitis.
 - Omega-3-acid ethyl esters represent an alternative to fibric acid derivatives and niacin for the treatment of hypertriglyceridemia.
- Other Key Facts:
 - Prescription niacin is approved by the Food and Drug Administration (FDA) for the treatment of hypertriglyceridemia.
 - Prescription niacin is also approved for the treatment of primary hypercholesterolemia and mixed dyslipidemia.^{4,5}
 - Niacin is available over-the-counter in immediate-release and sustained-release formulations.
 - Niacin is also available by prescription as immediate-release (Niacor[®]) and extended-release (Niaspan[®]) formulations.

References

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