

## Indiana Medicaid Therapeutics Committee Therapeutic Class Review Summary

### **Therapeutic Class:** Other Lipotropics

#### **Overview:**

Five agents, ezetimibe, ezetimibe/simvastatin, lovastatin/niacin ER, simvastatin/niacin ER, and niacin, are included in this therapeutic class review to distinguish them from the other subcategories within the lipotropic class. The agents in this review represent an agent with a unique mechanism of action, two combination products, and a B-complex vitamin.

Ezetimibe (FDA approved 2002) is an oral antilipemic agent approved for use as monotherapy or in conjunction with HMG CoA reductase inhibitors (statins) or fenofibrate. Ezetimibe reduces blood cholesterol by inhibiting the absorption of cholesterol within the small intestine. It localizes and appears to act at the brush border of the small intestine. The inhibition of cholesterol absorption leads to a decrease in the delivery of intestinal cholesterol to the liver. This causes a reduction of hepatic cholesterol stores and an increase in clearance of cholesterol from the blood. As monotherapy, ezetimibe exerts only a modest effect on lipid parameters. However, when ezetimibe is used in combination with a statin, the effects of the combination are greater than those of either agent used alone. Vytorin<sup>®</sup> is a combination product containing ezetimibe and simvastatin (a HMG CoA reductase inhibitor).

Niacin, a B-complex vitamin, was the first lipotropic agent shown to decrease the incidence of secondary myocardial infarction (MI) and reduce total mortality in MI patients. Some dosage forms are available without a prescription. The FDA officially approved niacin in 1938. The mechanism of action of its antilipemic effect is unknown but is unrelated to its biochemical role as a vitamin. One of its primary actions is decreased hepatic synthesis of VLDL-C (triglycerides). Several mechanisms have been proposed: inhibition of free fatty acid release from adipose tissue, increased lipoprotein lipase activity, decreased triglyceride synthesis, decreased VLDL-triglyceride transport, and an inhibition of lipolysis. Niaspan<sup>®</sup> has been reformulated as a film coated tablet, which is designed to slow the release of niacin and help reduce the incidence of flushing. Advicor<sup>®</sup> contains lovastatin (immediate-release) and niacin (extended-release). Due to the individual actions of lovastatin and niacin, Advicor<sup>®</sup> reduces LDL-cholesterol (30-42%) and triglycerides (32-44%), and increases HDL-cholesterol (20-30%). Simcor<sup>®</sup>, a combination of simvastatin and extended-release niacin recently approved by the FDA, provides greater reductions in LDL-cholesterol, total cholesterol, and triglycerides, and increases in HDL-cholesterol than simvastatin alone. Pravigard<sup>™</sup> PAC (pravastatin/buffered aspirin) has been discontinued by the manufacturer and is no longer available.

<b>Generic Name</b>	<b>Brand Name</b>	<b>Manufacturer</b>	<b>Generic Available</b>
Ezetimibe	Zetia <sup>®</sup>	Merck/Schering Plough	No
Ezetimibe/Simvastatin	Vytorin <sup>®</sup>	Merck/Schering Plough	No
Lovastatin/Niacin ER	Advicor <sup>®</sup>	Abbott Laboratories	No
Niacin	Niacor <sup>®</sup> , Niaspan <sup>®</sup>	Upsher-Smith, KOS Pharmaceuticals	Yes (Niacor <sup>®</sup> ) No (Niaspan <sup>®</sup> )
Niacin ER/Simvastatin	Simcor <sup>®</sup>	Abbott Laboratories	No

#### **Conclusion**

Lifestyle and dietary changes and optimal dosing of statins remain first line therapy for the treatment of hypercholesterolemia. Ezetimibe may be best reserved for patients who, after being treated with the maximum dose of a statin, require additional LDL lowering to reach the NCEP ATP III target.<sup>7-8, 13</sup> Ezetimibe may also be used in combination with fenofibrate. The combination of ezetimibe with simvastatin results in synergistic cholesterol-lowering effects.

When ezetimibe is used in combination with 10-80 mg of simvastatin, LDL-C reductions > 51% can be achieved, compared to LDL-C reductions of 36-40% with simvastatin monotherapy. The adverse effect profile for combined ezetimibe/statin therapy is similar to statin monotherapy, except for an increase in the incidence of hepatic enzyme elevations observed with combined ezetimibe/statin therapy. Vytorin™ provides an ezetimibe/statin (simvastatin) combination in one tablet, and is cost-effective, based on average wholesale costs, compared to taking the individual drugs separately. Niacin may be added to the optimal dose of a statin when additional increases in HDL-C are necessary. Some sustained-release niacin formulations have a lower incidence of flushing but a higher incidence of hepatotoxicity when compared to immediate-release dosage forms. More studies are needed to determine the place in therapy of a fixed dose lovastatin/niacin extended-release product.