



Indiana Medicaid Therapeutics Committee **Therapeutic Class Review Summary**

Therapeutic Class:

Omega-3 Polyunsaturated Fatty Acids

Overview:

Lovaza™ is indicated as an adjunct to diet to reduce very high (≥ 500 mg/dL) triglyceride concentrations in adult patients. This agent should be prescribed only after failure of nonpharmacologic measures, and should be used as an adjunct to these measures, including dietary modifications, and not a substitute for changing dietary habits. Lovaza™ received FDA approval in November 2004 and became commercially available in 2005 as Omacor®. The name was changed at the request of the FDA in June 2007 to avoid dispensing errors with Amicar®. Lovaza™ contains omega-3-acid ethyl esters, predominantly eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA). Although the exact mechanism of action is not understood, it is thought to inhibit acyl CoA:1,2-diacylglycerol acyltransferase and increase peroxisomal beta-oxidation in the liver, resulting in a decrease in triglycerides. It may also reduce the synthesis of triglycerides in the liver because EPA and DHA are poor substrates for the enzymes responsible for triglyceride synthesis.

The most common adverse effects associated with Lovaza™ use during clinical trials were back pain, flu-like syndrome, infection, pain, angina pectoris, dyspepsia, eructation, rash, and taste perversion. All occurred in less than 5% of patients, and at an incidence similar to that observed with placebo. Prolonged bleeding time has been observed in some studies with omega-3-acids; however, bleeding times did not exceed normal limits or produce clinically significant bleeding episodes. Patients taking Lovaza™ concomitantly with anticoagulants should receive periodic monitoring since clinical studies have not assessed the potential for a drug interaction. Clinically important drug interactions due to inhibition of cytochrome P-450-mediated metabolism are not anticipated. The usual dose of Lovaza™ is 4 g per day and may be administered in a single 4-g dose or as two 2-g doses. Lovaza™ is available as 1-g soft-gelatin capsules and contains at least 900 mg of the ethyl esters of omega-3 fatty acids, predominantly as a combination of the ethyl esters of EPA (approximately 465 mg) and DHA (approximately 375 mg). Lovaza™ was compared in clinical trials to both placebo and gemfibrozil and appears to be as effective as gemfibrozil for triglyceride lowering. Stalenhoef and coworkers conducted a randomized, double-blind, double-dummy clinical trial to evaluate the efficacy of Lovaza™ 4



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g/day compared to gemfibrozil 1200 mg/day in patients with primary hypertriglyceridemia. Patients in both treatment groups experienced significantly reduced total triglyceride levels in plasma and in the VLDL fraction. Lovaza™ plus simvastatin was compared to placebo plus simvastatin in a recent clinical trial, and demonstrated significant reductions in non-HDL-C, TG, VLDL-C, LDL-C, and TC/HDL-C ratio. A significant increase in HDL-C was also seen with the Lovaza plus simvastatin regimen.

Generic Name	Brand Name	Manufacturer
Omega-3-acid ethyl esters	Lovaza™	Reliant Pharmaceuticals

Summary:

At this time, Lovaza™ should be considered as a second-line therapy for hypertriglyceridemia due to the lack of outcome data. However, it may provide an alternative to fibric acid derivatives or HMG CoA reductase inhibitors when these agents are not well tolerated or for use in combination with these agents if additional triglyceride lowering is needed.