



Therapeutic Class ReviewSM

Omega-3 acid ethyl esters (Omacor[®])

February 2006

New Product for Review:
omega-3 ethyl esters (Omacor[®]) - Reliant

Dossier Provided by Manufacturer: Yes

Available Therapeutic Alternatives:

Preferred/Formulary	Non-Preferred/Non-Formulary
<u>Fibric acid derivatives:</u>	
gemfibrozil (Lopid [®]) [generics]	
fenofibrate (Lofibra [®]) [Gate Pharmaceuticals]	
<u>HMG CoA reductase inhibitors ('statins'):</u>	
fluvastatin (Lescol [®] , Lescol XL [®]) [Novartis]	atorvastatin (Lipitor [®]) [Pfizer]
lovastatin (Mevacor [®]) [generics]	pravastatin (Pravachol [®]) [Bristol-Myers-Squibb]
rosuvastatin (Crestor [®]) [AstraZeneca]	simvastatin (Zocor [®]) [Merck]
<u>Nicotinic acid derivatives:</u>	
niacin ERT (Niaspan [®]) [Kos Pharmaceuticals]	
<u>Combination Products:</u>	
simvastatin/ezetimibe (Vytorin [®]) [Merck/Schering-Plough]	lovastatin/niacin (Advicor [®]) [Kos Pharmaceuticals]

Reason for Review

- Determine preferred/formulary status for Omacor, a prescription strength fish oil supplement indicated for hypertriglyceridemia.

Executive Summary

- Omacor (omega-3 fatty acid esters):
 - Is a prescription product indicated for treatment of very high triglycerides (TG > 500mg/dl).
 - Contains high concentrations (at least 90%) of eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), two omega-3 fatty acids found in cold water fish and nutritional fish oil supplements.
 - Is approved in 14 countries for treatment of hypertriglyceridemia.
- Omacor is likely to be promoted for:
 - Its reduction of serum triglycerides and its tolerability.
 - Delivering a pure, consistent dose of omega-3 fatty acids.
 - Eliminating concerns of environmental toxins, such as mercury and PCBs.

Evidence:

- The evidence for Omacor is uncertain due to concerns with the validity of the studies.
- There is no useful or possibly useful evidence demonstrating that Omacor is as good as fibrates or niacin in the treatment of hypertriglyceridemia.
- There is currently no evidence that Omacor decreases the risk of cardiovascular events.
- In addition:
 - The potential risk associated with the elevation in LDL-C levels seen with Omacor is not known.
 - The effects of Omacor on HDL-C (good cholesterol) are uncertain and inconsistent.
- The safety of Omacor relative to alternative treatment options is not known.
 - There are no safety studies comparing Omacor with fibrates or niacin.
 - There are no studies that differentiate impurities between Omacor and other fish oil products.
- The incremental benefit of adding Omacor to existing 'statin' therapy is uncertain.

Conclusion:

- Omega-3 acid ethyl esters (Omacor) is non-preferred/non-formulary because:
 - There is no evidence that it provides additional clinical value over available treatment options for the treatment of hypertriglyceridemia.
 - There is potential for overuse of this product.

Products

Drug Product	Date of FDA Approval	FDA Approved Indications	Dose/Route	AWP* Cost or MAC†	Potential Off-Label Uses	
fenofibrate, micronized (Lofibra®) ¹	9/2001 (Tricor®)	1. Hypercholesterolemia 2. Hypertriglyceridemia	54 to 160 mg p.o. daily	\$27 to \$81	All of these medications have the potential for off-label use in conditions that arise as a result of abnormal lipid homeostasis, regardless of the specific indication for which they are approved. Additionally, off-label uses specifically related to Omacor may include cystic fibrosis ¹³ , and intermittent claudication ¹⁴ .	
gemfibrozil (generics) ²	12/1981	1. Hypertriglyceridemia (type IV and V) 2. Reduce the risk of developing coronary heart disease (type IIb patients)	600 mg p.o. b.i.d.	\$14		
niacin ERT (Niaspan®) ³	7/1997	1. Primary hypercholesterolemia 2. Mixed dyslipidemia (type IIa & IIb)	1 to 2 Gm p.o. daily	\$94 to \$188		
omega-3-acid ethyl esters (Omacor®) ⁴	11/2004	1. Reduce very high triglyceride (TG ≥ 500 mg/dl) levels in adults	2 Gm p.o. b.i.d.	\$142		
HMG CoA reductase inhibitors ('statins'):						
atorvastatin (Lipitor®) ⁵	12/1996	1. Prevention of cardiovascular disease 2. Hypercholesterolemia	10 to 80 mg p.o. daily	\$82 to \$118		
fluvastatin (Lescol®, Lescol XL®) ⁶	12/1993 10/2000 (XL)	1. Hypercholesterolemia and mixed dyslipidemia 2. Secondary prevention of coronary events 3. Atherosclerosis	20 to 40 mg p.o. b.i.d. 80 mg p.o. daily (XL)	\$132 \$85		
lovastatin (generics) ⁷	8/1987	1. Primary prevention of coronary heart disease 2. Coronary heart disease 3. Hypercholesterolemia 4. Adolescent patients with heterozygous familial hypercholesterolemia	10 to 80 mg p.o. daily	\$15 to \$70		
lovastatin/niacin (Advicor®) ⁸ - 20/500 mg - 20/1000 mg	11/2001	1. Primary hypercholesterolemia 2. Mixed dyslipidemia (type IIa & IIb) (not indicated for initial therapy)	1 tablet p.o. qHS	\$82 to \$87		
pravastatin (Pravachol®) ⁹	10/1991	1. Primary prevention of coronary events 2. Secondary prevention of cardiovascular events 3. Hyperlipidemia (primary, mixed dyslipidemias, high triglycerides)	20 to 80 mg p.o. daily	\$105 to \$154		
rosuvastatin (Crestor®) ¹⁰	8/2003	1. Primary hypercholesterolemia and mixed dyslipidemia 2. Elevated triglycerides (type IV) 3. Homozygous familial hypercholesterolemia	5 to 40 mg p.o. daily	\$93		
simvastatin (Zocor®) ¹¹	12/1991	1. Reductions in risk of CHD mortality and cardiovascular events 2. Hypercholesterolemia 3. Heterozygous familial hypercholesterolemia	10 to 80 mg p.o. daily	\$89 to \$155		
ezetimibe/simvastatin (Vytorin®) ¹² - 10/10mg - 10/20mg - 10/40mg - 10/80 mg	7/2004	1. Primary hypercholesterolemia 2. Homozygous familial hypercholesterolemia	1 tablet p.o. daily	\$108		

* AWP (average wholesale price) based on First Data Bank as of November 2005 for 30 days of therapy.

† MAC (Maximum Allowable Cost) based on The Regence Group maximum allowable cost as of October 2005 for 30 days of therapy.

Table 1: Lipid parameter changes seen with specific dyslipidemias¹⁵

	Dyslipidemia type					
	I	IIa	IIb	III	IV	V
Lipids elevated:						
Cholesterol	N to ↑	↑↑	↑↑	N to ↑↑	N to ↑	N to ↑↑
Triglycerides	↑↑	N	↑↑	N to ↑↑	↑↑	↑↑
Lipoproteins elevated:						
Chylomicrons	↑↑	N	N	N	N	↑↑
VLDL (pre-beta)	N to ↑	N to ↓↓	↑↑	N to ↑	↑↑	↑↑
LDL (beta)	↓↓	↑↑	↑↑	↑↑	N to ↓	↓↓
HDL (alpha)	↓↓	N	N	N	N to ↓	↓↓

N = normal ↑ = slight increase ↑↑ = increase ↓ = slight decrease ↓↓ = decrease

Table 2: Medications approved for treatment of specific dyslipidemias¹⁵

Treatment Options:	Dyslipidemia type					
	I	IIa	IIb	III	IV	V
atorvastatin (Lipitor [®]) ^{NP}		√	√	√	√	
fenofibrate (Lofibra [®])		√	√		√	√
fluvastatin (Lescol [®])		√	√			
gemfibrozil (Lopid [®])			√ ^a		√	√
lovastatin (Mevacor [®])		√	√			
lovastatin/niacin (Advicor [®]) ^{NP}		√	√			
niacin ERT (Niaspan [®])		√	√		√	√
omega-3 ethyl esters (Omacor [®]) ^{NP}			√ ^b		√ ^b	√ ^b
pravastatin (Pravachol [®]) ^{NP}		√	√	√	√	
rosuvastatin (Crestor [®])		√	√		√	
simvastatin (Zocor [®]) ^{NP}		√	√	√	√	
ezetimibe/simvastatin (Vytorin [®])		√ ^c	√ ^c	√ ^c	√ ^c	

NP = non-preferred/non-formulary

^a for patients without a history or symptoms of coronary heart disease, have failed bile acid sequestrants, and have low HDL, high LDL and high triglycerides.

^b FDA approved for very high triglycerides (≥ 500 mg/dl); risk may offset benefit in type IIb and type IV patients.

^c for mixed hyperlipidemia per prescribing information.

Table 3: Effect of various treatments on selected lipids and lipoproteins ¹⁶

Treatment	LDL	HDL	Triglycerides
Fibrates (gemfibrozil, fenofibrate)	↓ 5-20%*	↑ 10-35% [†]	↓ 20-50%
Nicotinic acid (niacin)	↓ 5-25%	↑ 15-35%	↓ 20-50%
Omacor [#] [17,18]	↑ 16-32%	↑ 6-13%	↓ 39-45%
'Statins' (lovastatin, fluvastatin, rosuvastatin)	↓ 18-55%	↑ 5-15%	↓ 7-30%

* may increase in hypertriglyceridemic patients.

[†] may see greater increases in patients with severe hypertriglyceridemia.

[#] based on two trials (Harris, et al. 1997, and Ponwell, et al. 1999) in patients with severe hypertriglyceridemia (TG ≥ 500 mg/dl).

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