

**HIGHLIGHTS OF PRESCRIBING INFORMATION**

**These highlights do not include all the information needed to use LOVAZA safely and effectively. See full prescribing information for LOVAZA.**

**LOVAZA (omega-3-acid ethyl esters) Capsules**

**Initial U.S. Approval: 2004**

**INDICATIONS AND USAGE**

LOVAZA is a combination of ethyl esters of omega 3 fatty acids, principally EPA and DHA, indicated as an adjunct to diet to reduce triglyceride (TG) levels in adult patients with severe ( $\geq 500$  mg/dL) hypertriglyceridemia. (1)

Limitations of Use: The effect of LOVAZA on cardiovascular mortality and morbidity in patients with elevated triglycerides has not been determined. (1)

**DOSAGE AND ADMINISTRATION**

- The daily dose of LOVAZA is 4 grams per day taken as a single 4-gram dose (4 capsules) or as two 2-gram doses (2 capsules given twice daily). (2)
- Patients should be advised to swallow LOVAZA capsules whole. Do not break open, crush, dissolve or chew LOVAZA. (2)

**DOSAGE FORMS AND STRENGTHS**

1-gram transparent soft-gelatin capsules. (3)

**CONTRAINDICATIONS**

LOVAZA is contraindicated in patients with known hypersensitivity (e.g., anaphylactic reaction) to LOVAZA or any of its components. (4)

**WARNINGS AND PRECAUTIONS**

- In patients with hepatic impairment, monitor ALT and AST levels periodically during therapy. (5.1)

- LOVAZA may increase levels of LDL. Monitor LDL levels periodically during therapy. (5.1)
- Use with caution in patients with known hypersensitivity to fish and/or shellfish. (5.2)

**ADVERSE REACTIONS**

The most common adverse events (incidence  $>3\%$  and greater than placebo) were eructation, infection, flu syndrome, and dyspepsia. (6)

**To report SUSPECTED ADVERSE REACTIONS, contact GlaxoSmithKline at 1-888-825-5249 or FDA at 1-800-FDA-1088 or [www.fda.gov/medwatch](http://www.fda.gov/medwatch).**

**DRUG INTERACTIONS**

Omega-3-acids may prolong bleeding time. Patients taking LOVAZA and an anticoagulant or other drug affecting coagulation should be monitored periodically. (7.1)

**USE IN SPECIFIC POPULATIONS**

- Pregnancy: Use during pregnancy only if the potential benefit justifies the potential risk to the fetus. (8.1)
- Pediatric Use: The safety and effectiveness in pediatric patients have not been established. (8.4)

**See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.**

**Revised: Month Year  
LVZ:XPI**

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\*Sections or subsections omitted from the full prescribing information are not listed.

1 **FULL PRESCRIBING INFORMATION**

2 **1 INDICATIONS AND USAGE**

3 LOVAZA<sup>®</sup> (omega-3-acid ethyl esters) is indicated as an adjunct to diet to reduce  
4 triglyceride (TG) levels in adult patients with severe ( $\geq 500$  mg/dL) hypertriglyceridemia.

5 **Usage Considerations:** Patients should be placed on an appropriate lipid-lowering diet  
6 before receiving LOVAZA and should continue this diet during treatment with LOVAZA.

7 Laboratory studies should be done to ascertain that the lipid levels are consistently  
8 abnormal before instituting LOVAZA therapy. Every attempt should be made to control serum  
9 lipids with appropriate diet, exercise, weight loss in obese patients, and control of any medical  
10 problems such as diabetes mellitus and hypothyroidism that are contributing to the lipid  
11 abnormalities. Medications known to exacerbate hypertriglyceridemia (such as beta blockers,  
12 thiazides, estrogens) should be discontinued or changed if possible prior to consideration of  
13 triglyceride-lowering drug therapy.

14 **Limitations of Use:** The effect of LOVAZA on cardiovascular mortality and morbidity  
15 in patients with elevated triglycerides has not been determined.

16 **2 DOSAGE AND ADMINISTRATION**

- 17 • Assess triglyceride levels carefully before initiating therapy. Identify other causes (e.g.,  
18 diabetes mellitus, hypothyroidism, or medications) of high triglyceride levels and manage as  
19 appropriate. [see *Indications and Usage (1)*].  
20 • Patients should be placed on an appropriate lipid-lowering diet before receiving LOVAZA,  
21 and should continue this diet during treatment with LOVAZA. In clinical studies, LOVAZA  
22 was administered with meals.

23 The daily dose of LOVAZA is 4 grams per day. The daily dose may be taken as a single  
24 4-gram dose (4 capsules) or as two 2-gram doses (2 capsules given twice daily).

25 Patients should be advised to swallow LOVAZA capsules whole. Do not break open,  
26 crush, dissolve or chew LOVAZA.

27 **3 DOSAGE FORMS AND STRENGTHS**

28 LOVAZA (omega-3-acid ethyl esters) capsules are supplied as 1-gram transparent soft-  
29 gelatin capsules filled with light-yellow oil and bearing the designation REL900.

30 **4 CONTRAINDICATIONS**

31 LOVAZA is contraindicated in patients with known hypersensitivity (e.g., anaphylactic  
32 reaction) to LOVAZA or any of its components.

33 **5 WARNINGS AND PRECAUTIONS**

34 **5.1 Monitoring: Laboratory Tests**

35 In patients with hepatic impairment, alanine aminotransferase (ALT) and aspartate  
36 aminotransferase (AST) levels should be monitored periodically during therapy with LOVAZA.  
37 In some patients, increases in ALT levels without a concurrent increase in AST levels were  
38 observed.

39 In some patients, LOVAZA increases LDL-C levels. LDL-C levels should be monitored  
40 periodically during therapy with LOVAZA.

41 Laboratory studies should be performed periodically to measure the patient's TG levels  
42 during therapy with LOVAZA.

43 **5.2 Fish Allergy**

44 LOVAZA contains ethyl esters of omega-3 fatty acids (EPA and DHA) obtained from the  
45 oil of several fish sources. It is not known whether patients with allergies to fish and/or shellfish,  
46 are at increased risk of an allergic reaction to LOVAZA. LOVAZA should be used with caution  
47 in patients with known hypersensitivity to fish and/or shellfish.

48 **6 ADVERSE REACTIONS**

49 **6.1 Clinical Trials Experience**

50 Because clinical trials are conducted under widely varying conditions, adverse reaction  
51 rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical  
52 trials of another drug and may not reflect the rates observed in practice.

53 Adverse events reported in at least 1% of patients treated with LOVAZA 4 grams per day  
54 or placebo during 8 randomized, placebo-controlled, double-blind, parallel-group studies for  
55 HTG are listed in Table 1. Adverse events led to discontinuation of treatment in 3.5% of patients  
56 treated with LOVAZA and 2.6% of patients treated with placebo.

57  
58  
59

**Table 1. Adverse Events in Randomized, Placebo-Controlled, Double-Blind, Parallel-Group Studies for Very High TG Levels ( $\geq 500$  mg/dL) that used LOVAZA**

<b>BODY SYSTEM Adverse Event*</b>	<b>LOVAZA 4 grams/day (N = 226)</b>		<b>Placebo (N = 228)</b>	
	<b>n</b>	<b>%</b>	<b>n</b>	<b>%</b>
Subjects with at least 1 adverse event	80	35.4	63	27.6
Body as a whole				
Infection	10	4.4	5	2.2
Flu syndrome	8	3.5	3	1.3
Back pain	5	2.2	3	1.3
Pain	4	1.8	3	1.3
Cardiovascular				
Angina pectoris	3	1.3	2	0.9
Digestive				
Eructation	11	4.9	5	2.2
Dyspepsia	7	3.1	6	2.6
Skin				
Rash	4	1.8	1	0.4
Special senses				
Taste perversion	6	2.7	0	0.0

60 \* Adverse events were coded using COSTART, version 5.0. Subjects were counted only once for  
61 each body system and for each preferred term.

62

63 Additional adverse events reported by 1 or more patients from clinical studies for HTG  
64 are listed below:

65 *Body as a Whole:* Enlarged abdomen, asthenia, body odor, chest pain, chills, suicide,  
66 fever, generalized edema, fungal infection, malaise, neck pain, neoplasm, rheumatoid arthritis,  
67 and sudden death.

68 *Cardiovascular System:* Arrhythmia, bypass surgery, cardiac arrest, hyperlipemia,  
69 hypertension, migraine, myocardial infarct, myocardial ischemia, occlusion, peripheral vascular  
70 disorder, syncope, and tachycardia.

71 *Digestive System:* Anorexia, constipation, dry mouth, dysphagia, colitis, fecal  
72 incontinence, gastritis, gastroenteritis, gastrointestinal disorder, increased appetite, intestinal  
73 obstruction, melena, pancreatitis, tenesmus, and vomiting.

74 *Hematologic-Lymphatic System:* Lymphadenopathy.

75 *Infections and Infestations:* Viral infection.

76 *Metabolic and Nutritional Disorders:* Edema, hyperglycemia, increased ALT, and  
77 increased AST.

78            *Musculoskeletal System:* Arthralgia, arthritis, myalgia, pathological fracture, and tendon  
79 disorder.

80            *Nervous System:* Central nervous system neoplasia, depression, dizziness, emotional  
81 lability, facial paralysis, insomnia, vasodilatation, and vertigo.

82            *Respiratory System:* Asthma, bronchitis, increased cough, dyspnea, epistaxis, laryngitis,  
83 pharyngitis, pneumonia, rhinitis, and sinusitis.

84            *Skin:* Alopecia, eczema, pruritus, and sweating.

85            *Special Senses:* Cataract.

86            *Urogenital System:* Cervix disorder, endometrial carcinoma, epididymitis, and  
87 impotence.

## 88 **6.2 Postmarketing Experience**

89            In addition to adverse reactions reported from clinical trials, the events described below  
90 have been identified during post-approval use of LOVAZA. Because these events are reported  
91 voluntarily from a population of unknown size, it is not possible to reliably estimate their  
92 frequency or to always establish a causal relationship to drug exposure.

93            The following events have been reported: anaphylactic reaction, hemorrhagic diathesis.

## 94 **7 DRUG INTERACTIONS**

### 95 **7.1 Anticoagulants or Other Drugs Affecting Coagulation**

96            Some studies with omega-3-acids demonstrated prolongation of bleeding time. The  
97 prolongation of bleeding time reported in these studies has not exceeded normal limits and did  
98 not produce clinically significant bleeding episodes. Clinical studies have not been done to  
99 thoroughly examine the effect of LOVAZA and concomitant anticoagulants. Patients receiving  
100 treatment with LOVAZA and an anticoagulant or other drug affecting coagulation should be  
101 monitored periodically (e.g., aspirin, NSAIDS, warfarin, coumarin).

## 102 **8 USE IN SPECIFIC POPULATIONS**

### 103 **8.1 Pregnancy**

104            Pregnancy Category C: There are no adequate and well-controlled studies in pregnant  
105 women. It is unknown whether LOVAZA can cause fetal harm when administered to a pregnant  
106 woman or can affect reproductive capacity. LOVAZA should be used during pregnancy only if  
107 the potential benefit to the patient justifies the potential risk to the fetus.

108            Animal Data: Omega-3-acid ethyl esters have been shown to have an embryocidal effect  
109 in pregnant rats when given in doses resulting in exposures 7 times the recommended human  
110 dose of 4 grams/day based on a body surface area comparison.

111            In female rats given oral gavage doses of 100, 600, and 2,000 mg/kg/day beginning 2  
112 weeks prior to mating and continuing through gestation and lactation, no adverse effects were  
113 observed in the high dose group (5 times human systemic exposure following an oral dose of 4  
114 grams/day based on body surface area comparison).

115 In pregnant rats given oral gavage doses of 1,000, 3,000, and 6,000 mg/kg/day from  
116 gestation day 6 through 15, no adverse effects were observed (14 times human systemic  
117 exposure following an oral dose of 4 grams/day based on a body surface area comparison).

118 In pregnant rats given oral gavage doses of 100, 600, and 2,000 mg/kg/day from gestation  
119 day 14 through lactation day 21, no adverse effects were seen at 2,000 mg/kg/day (5 times the  
120 human systemic exposure following an oral dose of 4 grams/day based on a body surface area  
121 comparison). However, decreased live births (20% reduction) and decreased survival to postnatal  
122 day 4 (40% reduction) were observed in a dose-ranging study using higher doses of 3,000  
123 mg/kg/day (7 times the human systemic exposure following an oral dose of 4 grams/day based  
124 on a body surface area comparison).

125 In pregnant rabbits given oral gavage doses of 375, 750, and 1,500 mg/kg/day from  
126 gestation day 7 through 19, no findings were observed in the fetuses in groups given 375  
127 mg/kg/day (2 times human systemic exposure following an oral dose of 4 grams/day based on a  
128 body surface area comparison). However, at higher doses, evidence of maternal toxicity was  
129 observed (4 times human systemic exposure following an oral dose of 4 grams/day based on a  
130 body surface area comparison).

### 131 **8.3 Nursing Mothers**

132 It is not known whether omega-3-acid ethyl esters are excreted in human milk. Because  
133 many drugs are excreted in human milk, caution should be exercised when LOVAZA is  
134 administered to a nursing woman.

### 135 **8.4 Pediatric Use**

136 Safety and effectiveness in pediatric patients have not been established.

### 137 **8.5 Geriatric Use**

138 A limited number of patients older than 65 years were enrolled in the clinical studies of  
139 LOVAZA. Safety and efficacy findings in subjects older than 60 years did not appear to differ  
140 from those of subjects younger than 60 years.

## 141 **9 DRUG ABUSE AND DEPENDENCE**

142 LOVAZA does not have any known drug abuse or withdrawal effects.

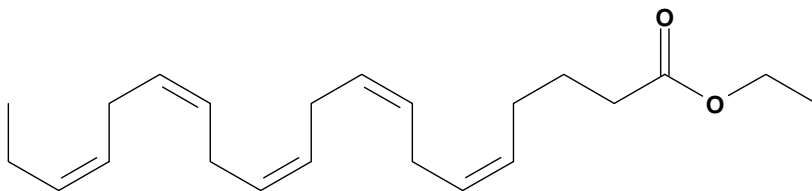
## 143 **10 OVERDOSAGE**

144 In the event of an overdose, the patient should be treated symptomatically, and general  
145 supportive care measures instituted, as required.

## 146 **11 DESCRIPTION**

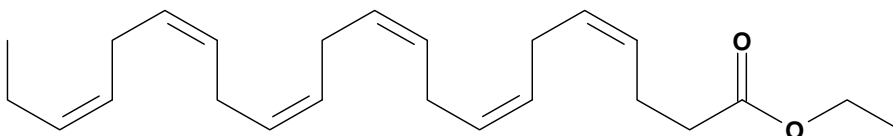
147 LOVAZA, a lipid-regulating agent, is supplied as a liquid-filled gel capsule for oral  
148 administration. Each 1-gram capsule of LOVAZA contains at least 900 mg of the ethyl esters of  
149 omega-3 fatty acids sourced from fish oils. These are predominantly a combination of ethyl  
150 esters of eicosapentaenoic acid (EPA - approximately 465 mg) and docosahexaenoic acid (DHA  
151 - approximately 375 mg).

152 The empirical formula of EPA ethyl ester is  $C_{22}H_{34}O_2$ , and the molecular weight of EPA  
153 ethyl ester is 330.51. The structural formula of EPA ethyl ester is:



154  
155

156 The empirical formula of DHA ethyl ester is  $C_{24}H_{36}O_2$ , and the molecular weight of DHA  
157 ethyl ester is 356.55. The structural formula of DHA ethyl ester is:



158  
159

160 LOVAZA capsules also contain the following inactive ingredients: 4 mg  $\alpha$ -tocopherol (in  
161 a carrier of soybean oil), and gelatin, glycerol, and purified water (components of the capsule  
162 shell).

## 163 **12 CLINICAL PHARMACOLOGY**

### 164 **12.1 Mechanism of Action**

165 The mechanism of action of LOVAZA is not completely understood. Potential  
166 mechanisms of action include inhibition of acyl-CoA:1,2-diacylglycerol acyltransferase,  
167 increased mitochondrial and peroxisomal  $\beta$ -oxidation in the liver, decreased lipogenesis in the  
168 liver, and increased plasma lipoprotein lipase activity. LOVAZA may reduce the synthesis of  
169 triglycerides in the liver because EPA and DHA are poor substrates for the enzymes responsible  
170 for TG synthesis, and EPA and DHA inhibit esterification of other fatty acids.

### 171 **12.3 Pharmacokinetics**

172 In healthy volunteers and in patients with hypertriglyceridemia, EPA and DHA were  
173 absorbed when administered as ethyl esters orally. Omega-3-acids administered as ethyl esters  
174 (LOVAZA) induced significant, dose-dependent increases in serum phospholipid EPA content,  
175 though increases in DHA content were less marked and not dose-dependent when administered  
176 as ethyl esters.

177 **Specific Populations: Age:** Uptake of EPA and DHA into serum phospholipids in  
178 subjects treated with LOVAZA was independent of age (<49 years versus  $\geq$ 49 years).

179 **Gender:** Females tended to have more uptake of EPA into serum phospholipids than  
180 males. The clinical significance of this is unknown.

181 **Pediatric:** Pharmacokinetics of LOVAZA in pediatric patients have not been  
182 established [see Use in Specific Populations (8.4)].

183 **Renal or Hepatic Impairment:** LOVAZA has not been studied in patients with renal  
184 or hepatic impairment.

185 **Drug-Drug Interactions:** *Simvastatin:* In a 14-day study of 24 healthy adult subjects,  
186 daily co-administration of simvastatin 80 mg with LOVAZA 4 grams did not affect the extent  
187 (AUC) or rate ( $C_{max}$ ) of exposure to simvastatin or the major active metabolite, beta-hydroxy  
188 simvastatin at steady state.

189 *Atorvastatin:* In a 14-day study of 50 healthy adult subjects, daily co-administration  
190 of atorvastatin 80 mg with LOVAZA 4 grams did not affect AUC or  $C_{max}$  of exposure to  
191 atorvastatin, 2-hydroxyatorvastatin, or 4-hydroxyatorvastatin at steady state.

192 *Rosuvastatin:* In a 14-day study of 48 healthy adult subjects, daily co-administration  
193 of rosuvastatin 40 mg with LOVAZA 4 grams did not affect AUC or  $C_{max}$  of exposure to  
194 rosuvastatin at steady state.

195 *In vitro* studies using human liver microsomes indicated that clinically significant  
196 cytochrome P450 mediated inhibition by EPA/DHA combinations are not expected in humans.

## 197 **13 NONCLINICAL TOXICOLOGY**

### 198 **13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility**

199 In a rat carcinogenicity study with oral gavage doses of 100, 600, and 2,000 mg/kg/day,  
200 males were treated with omega-3-acid ethyl esters for 101 weeks and females for 89 weeks  
201 without an increased incidence of tumors (up to 5 times human systemic exposures following an  
202 oral dose of 4 grams/day based on a body surface area comparison). Standard lifetime  
203 carcinogenicity bioassays were not conducted in mice.

204 Omega-3-acid ethyl esters were not mutagenic or clastogenic with or without metabolic  
205 activation in the bacterial mutagenesis (Ames) test with *Salmonella typhimurium* and  
206 *Escherichia coli* or in the chromosomal aberration assay in Chinese hamster V79 lung cells or  
207 human lymphocytes. Omega-3-acid ethyl esters were negative in the *in vivo* mouse micronucleus  
208 assay.

209 In a rat fertility study with oral gavage doses of 100, 600, and 2,000 mg/kg/day, males  
210 were treated for 10 weeks prior to mating and females were treated for 2 weeks prior to and  
211 throughout mating, gestation, and lactation. No adverse effect on fertility was observed at 2,000  
212 mg/kg/day (5 times human systemic exposure following an oral dose of 4 grams/day based on a  
213 body surface area comparison).

## 214 **14 CLINICAL STUDIES**

### 215 **14.1 Severe Hypertriglyceridemia**

216 The effects of LOVAZA 4 grams per day were assessed in 2 randomized, placebo-  
217 controlled, double-blind, parallel-group studies of 84 adult patients (42 on LOVAZA, 42 on  
218 placebo) with very high triglyceride levels. Patients whose baseline triglyceride levels were  
219 between 500 and 2,000 mg/dL were enrolled in these 2 studies of 6 and 16 weeks duration. The  
220 median triglyceride and LDL-C levels in these patients were 792 mg/dL and 100 mg/dL,  
221 respectively. Median HDL-C level was 23.0 mg/dL.

222 The changes in the major lipoprotein lipid parameters for the groups receiving LOVAZA  
223 or placebo are shown in Table 2.

224

225 **Table 2. Median Baseline and Percent Change From Baseline in Lipid Parameters in**  
226 **Patients with Very High TG Levels ( $\geq 500$  mg/dL)**

Parameter	LOVAZA N = 42		Placebo N = 42		Difference
	BL	% Change	BL	% Change	
TG	816	-44.9	788	+6.7	-51.6
Non-HDL-C	271	-13.8	292	-3.6	-10.2
TC	296	-9.7	314	-1.7	-8.0
VLDL-C	175	-41.7	175	-0.9	-40.8
HDL-C	22	+9.1	24	0.0	+9.1
LDL-C	89	+44.5	108	-4.8	+49.3

227 BL = Baseline (mg/dL); % Change = Median Percent Change from Baseline;

228 Difference = LOVAZA Median % Change – Placebo Median % Change

229

230 LOVAZA 4 grams per day reduced median TG, VLDL-C, and non-HDL-C levels and  
231 increased median HDL-C from baseline relative to placebo. Treatment with LOVAZA to reduce  
232 very high TG levels may result in elevations in LDL-C and non-HDL-C in some individuals.  
233 Patients should be monitored to ensure that the LDL-C level does not increase excessively.

234 The effect of LOVAZA on the risk of pancreatitis in patients with very high TG levels  
235 has not been evaluated.

236 The effect of LOVAZA on cardiovascular mortality and morbidity in patients with  
237 elevated TG levels has not been determined.

#### 238 **14.2 Other Clinical Experience**

239 The effects of LOVAZA 4 grams per day as add-on therapy to treatment with simvastatin  
240 were evaluated in a randomized, placebo-controlled, double-blind, parallel-group study of 254  
241 adult patients (122 on LOVAZA and 132 on placebo) with persistent high triglycerides (200 to  
242 499 mg/dL) despite simvastatin therapy. Patients were treated with open-label simvastatin 40 mg  
243 per day for 8 weeks prior to randomization to control their LDL-C to no greater than 10% above  
244 NCEP ATP III goal and remained on this dose throughout the study. Following 8 weeks of open-  
245 label treatment with simvastatin, patients were randomized to either LOVAZA 4 grams per day  
246 or placebo for an additional 8 weeks with simvastatin co-therapy. The median baseline  
247 triglyceride and LDL-C levels in these patients were 268 mg/dL and 89 mg/dL, respectively.  
248 Median baseline non-HDL-C and HDL-C levels were 138 mg/dL and 45 mg/dL, respectively.

249 The changes in the major lipoprotein lipid parameters for the groups receiving LOVAZA  
250 plus simvastatin or placebo plus simvastatin are shown in Table 3.

251

252 **Table 3. Response to the Addition of LOVAZA 4 grams per day to Ongoing Simvastatin**  
253 **40 mg per day Therapy in Patients with High Triglycerides (200 to 499 mg/dL)**

Parameter	LOVAZA + Simvastatin N = 122			Placebo + Simvastatin N = 132			Difference	P-Value
	BL	EOT	Median % Change	BL	EOT	Median % Change		
Non-HDL-C	137	123	-9.0	141	134	-2.2	-6.8	<0.0001
TG	268	182	-29.5	271	260	-6.3	-23.2	<0.0001
TC	184	172	-4.8	184	178	-1.7	-3.1	<0.05
VLDL-C	52	37	-27.5	52	49	-7.2	-20.3	<0.05
Apo-B	86	80	-4.2	87	85	-1.9	-2.3	<0.05
HDL-C	46	48	+3.4	43	44	-1.2	+4.6	<0.05
LDL-C	91	88	+0.7	88	85	-2.8	+3.5	=0.05

254 BL = Baseline (mg/dL); EOT = End of Treatment (mg/dL); Median % Change = Median Percent  
255 Change from Baseline; Difference = LOVAZA Median % Change – Placebo Median % Change  
256

257 LOVAZA 4 grams per day significantly reduced non-HDL-C, TG, TC, VLDL-C, and  
258 Apo-B levels and increased HDL-C and LDL-C from baseline relative to placebo.

259 **16 HOW SUPPLIED/STORAGE AND HANDLING**

260 LOVAZA (omega-3-acid ethyl esters) capsules are supplied as 1-gram transparent soft-  
261 gelatin capsules filled with light-yellow oil and bearing the designation REL900.

262 Bottles of 60: NDC 0173-0783-01

263 Bottles of 120: NDC 0173-0783-02

264

265 Store at 25°C (77°F); excursions permitted to 15° to 30°C (59° to 86°F) [see USP  
266 Controlled Room Temperature]. Do not freeze. Keep out of reach of children.

267 **17 PATIENT COUNSELING INFORMATION**

268 See FDA-approved patient labeling

269

- 270 • LOVAZA should be used with caution in patients with known sensitivity or allergy to fish  
271 and/or shellfish [see *Warnings and Precautions (5.3)*].
- 272 • Patients should be advised that use of lipid-regulating agents does not reduce the importance  
273 of adhering to diet [see *Dosage and Administration (2)*].
- 274 • Patients should be advised not to alter LOVAZA capsules in any way and to ingest intact  
275 capsules only [see *Dosage and Administration (2)*].

276

277 Manufactured for GlaxoSmithKline by:

278 Catalent Pharma Solutions

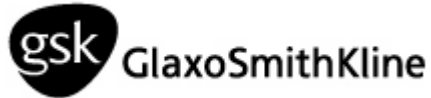
279 2725 Scherer Drive

280 St. Petersburg, FL 33716-1016

281  
282 Accucaps Industries Limited  
283 2125 Ambassador Drive  
284 Windsor, Ontario, Canada N9B 3R5

285  
286 Banner Pharmaceuticals Inc.  
287 4125 Premier Drive  
288 High Point, NC 27265

289  
290 Distributed by:



291  
292 GlaxoSmithKline  
293 Research Triangle Park, NC 27709

294  
295 LOVAZA is a registered trademark of the GlaxoSmithKline group of companies.

296  
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298 PHARMACIST-DETACH HERE AND GIVE INSTRUCTIONS TO PATIENT  
299 -----  
300

301 **PATIENT INFORMATION**  
302 **LOVAZA<sup>®</sup> (lō-vā-ză)**  
303 **(omega-3-acid ethyl esters) Capsules**  
304

305 Read the Patient Information that comes with LOVAZA before you start taking it, and each time  
306 you get a refill. There may be new information. This leaflet does not take the place of talking  
307 with your doctor about your condition or treatment.  
308

309 **What is LOVAZA?**

310 LOVAZA is a prescription medicine, called a lipid-regulating medicine, for adults. LOVAZA is  
311 made of omega-3 fatty acids from oils of fish, such as salmon and mackerel. Omega-3 fatty acids  
312 are substances that your body needs but cannot produce itself.  
313

314 LOVAZA is used along with a low-fat and low-cholesterol diet to lower very high triglycerides  
315 (fats) in your blood. Before taking LOVAZA, talk to your healthcare provider about how you  
316 can lower high blood fats by:

- 317 • losing weight, if you are overweight
- 318 • increasing physical exercise
- 319 • lowering alcohol use
- 320 • treating diseases such as diabetes and low thyroid (hypothyroidism)
- 321 • adjusting the dose or changing other medicines that raise triglyceride levels such as certain  
322 blood pressure medicines and estrogens  
323

324 Treatment with LOVAZA has not been shown to prevent heart attacks or strokes.  
325

326 LOVAZA has not been studied in children under the age of 18 years.  
327

328 **Who should not take LOVAZA?**

329 Do not take LOVAZA if you:

- 330 • **are allergic to LOVAZA or any of its ingredients.** See the end of this leaflet for a complete  
331 list of ingredients in LOVAZA.  
332

333 **What should I tell my doctor before taking LOVAZA?**

334 **Tell your doctor about all of your medical conditions, including if you:**

- 335 • drink more than 2 glasses of alcohol daily.
- 336 • have diabetes.
- 337 • have a thyroid problem called hypothyroidism.

- 338 • have a liver problem.
- 339 • have a pancreas problem.
- 340 • are allergic to fish and/or shellfish. LOVAZA may not be right for you.
- 341 • are pregnant, or planning to become pregnant. It is not known if LOVAZA can harm your
- 342 unborn baby.
- 343 • are breastfeeding. It is not known if LOVAZA passes into your milk and if it can harm your
- 344 baby.

345

346 Tell your doctor about all the medicines you take, including prescription and non-prescription  
347 medicine, vitamins, and herbal supplements. LOVAZA and certain other medicines can interact.  
348 Especially tell your doctor if you take medicines that affect clotting such as anticoagulants or  
349 blood thinners. Examples of these medicines include aspirin, nonsteroidal anti-inflammatory  
350 agents (NSAIDs), warfarin, coumarin, and clopidogrel (PLAVIX®).

351

352 Know all the medicines you take. Keep a list of them with you to show your doctor and  
353 pharmacist.

354

### 355 **How should I take LOVAZA?**

- 356 • Take LOVAZA exactly as prescribed. Do not change your dose or stop LOVAZA without
- 357 talking to your doctor.
- 358 • The usual dose of LOVAZA is 4 capsules:
  - 359 • Take all 4 capsules at the same time, or
  - 360 • Take 2 capsules two times a day
- 361 • Take LOVAZA at the same time or times each day.
- 362 • Take LOVAZA with or without food. You may find it easier to take LOVAZA with food.
- 363 • Do not take more than 4 capsules a day. Taking more than 4 capsules per day may increase
- 364 the chance of side effects.
- 365 • Take LOVAZA capsules whole. Do not break, crush, dissolve, or chew LOVAZA capsules
- 366 before swallowing. If you cannot swallow LOVAZA capsules whole, tell your doctor. You
- 367 may need a different medicine.
- 368 • Your doctor should start you on a low-fat and low-cholesterol diet before giving you
- 369 LOVAZA. Stay on this low-fat and low-cholesterol diet while taking LOVAZA.
- 370 • Your doctor should do blood tests to check your triglyceride and cholesterol levels during
- 371 treatment with LOVAZA.
- 372 • If you have liver disease, your doctor should do blood tests to check your liver function
- 373 during treatment with LOVAZA.
- 374 • If you miss a dose of LOVAZA, take it as soon as you remember. However, if you miss one
- 375 day of LOVAZA, do not double your dose when you next take it.
- 376 • If you take too much LOVAZA or overdose, call your doctor or Poison Control Center right
- 377 away.

378

379 **What are the possible side effects of LOVAZA?**

380 The most common side effects with LOVAZA are burping, infection, flu symptoms, upset  
381 stomach, a change in your sense of taste, back pain, and skin rash.

382

383 LOVAZA may affect certain blood tests. It may change:

- 384 • one of the tests to check liver function (ALT)
- 385 • one of the tests to measure cholesterol levels (LDL-C)

386

387 Talk to your doctor if you have side effects that bother you or that will not go away. You may  
388 report side effects to FDA at 1-800-FDA-1088.

389

390 These are not all the side effects with LOVAZA. For more information, ask your doctor or  
391 pharmacist.

392

393 **How should I store LOVAZA?**

- 394 • Store LOVAZA at room temperature, 59° to 86° F (15° to 30° C). Do not freeze.
- 395 • Do not keep medicine that is out of date or that you no longer need.
- 396 • **Keep LOVAZA out of the reach of children.** Be sure that if you throw medicines away, it  
397 is out of the reach of children.

398

399 **General information about LOVAZA**

400 Medicines are sometimes prescribed for conditions that are not mentioned in patient information  
401 leaflets. Do not use LOVAZA for a condition for which it was not prescribed. Do not give  
402 LOVAZA to other people, even if they have the same problem you have. It may harm them.

403

404 This leaflet summarizes the most important information about LOVAZA. If you would like more  
405 information, talk with your doctor. You can ask your doctor or pharmacist for information about  
406 LOVAZA that is written for health professionals or go to [www.LOVAZA.com](http://www.LOVAZA.com).

407

408 **What are the ingredients in LOVAZA?**

409 Active Ingredient: Omega-3-acid ethyl esters

410 Inactive Ingredients: Gelatin, glycerol, purified water, alpha-tocopherol (in soybean oil)

411

412 LOVAZA is a registered trademark of the GlaxoSmithKline group of companies.

413 PLAVIX is a registered trademark of Sanofi-Synthelabo.

414

415 Manufactured for GlaxoSmithKline by:

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