PRESCRIBING INFORMATION

- 1
- 2 LOVAZA®
- 3 (omega-3-acid ethyl esters)
- 4 Capsules

5 **DESCRIPTION**

- 6 LOVAZA, a lipid-regulating agent, is supplied as a liquid-filled gel capsule for oral
- 7 administration. Each 1-gram capsule of LOVAZA (omega-3-acid ethyl esters) contains at least
- 8 900 mg of the ethyl esters of omega-3 fatty acids. These are predominantly a combination of
- 9 ethyl esters of eicosapentaenoic acid (EPA approximately 465 mg) and docosahexaenoic acid
- 10 (DHA approximately 375 mg).
- 11 The structural formula of EPA ethyl ester is:



- 12
- 13 The empirical formula of EPA ethyl ester is $C_{22}H_{34}O_2$, and the molecular weight of EPA
- 14 ethyl ester is 330.51.
- 15 The structural formula of DHA ethyl ester is:



16

17 The empirical formula of DHA ethyl ester is $C_{24}H_{36}O_2$, and the molecular weight of DHA

- 18 ethyl ester is 356.55.
- 19 LOVAZA capsules also contain the following inactive ingredients: 4 mg α -tocopherol (in a
- 20 carrier of partially hydrogenated vegetable oils including soybean oil), and gelatin, glycerol, and
- 21 purified water (components of the capsule shell).

22 CLINICAL PHARMACOLOGY

- 23 Mechanism of Action: The mechanism of action of LOVAZA is not completely understood.
- 24 Potential mechanisms of action include inhibition of acyl CoA:1,2-diacylglycerol
- 25 acyltransferase, increased mitochondrial and peroxisomal β -oxidation in the liver, decreased
- 26 lipogenesis in the liver, and increased plasma lipoprotein lipase activity. LOVAZA may reduce
- 27 the synthesis of triglycerides (TGs) in the liver because EPA and DHA are poor substrates for the
- 28 enzymes responsible for TG synthesis, and EPA and DHA inhibit esterification of other fatty
- 29 acids.
- 30 Pharmacokinetic and Bioavailability Studies: In healthy volunteers and in patients with
- 31 hypertriglyceridemia (HTG), EPA and DHA were absorbed when administered as ethyl esters
- 32 orally. Omega-3-acids administered as ethyl esters (LOVAZA) induced significant, dose-

- 33 dependent increases in serum phospholipid EPA content, though increases in DHA content were
- 34 less marked and not dose-dependent when administered as ethyl esters. Uptake of EPA and DHA
- 35 into serum phospholipids in subjects treated with LOVAZA was independent of age (<49 years
- 36 versus ≥ 49 years). Females tended to have more uptake of EPA into serum phospholipids than
- 37 males. Pharmacokinetic data on LOVAZA in children are not available.
- 38 Drug Interactions: Cytochrome P450-Dependent Monooxygenase Activities: The
- 39 effect of a mixture of free fatty acids (FFA), EPA/DHA and their FFA-albumin conjugate on
- 40 cytochrome P450-dependent monooxygenase activities was assessed in human liver microsomes.
- 41 At the 23 micromole concentration, FFA resulted in a less than 32% inhibition of CYP1A2, 2A6,
- 42 2C9, 2C19, 2D6, 2E1, and 3A. At the 23 micromole concentration, the FFA-albumin conjugate
- 43 resulted in a less than 20% inhibition of CYP2A6, 2C19, 2D6, and 3A, with a 68% inhibition
- 44 being seen for CYP2E1. Since the free forms of the EPA and DHA are undetectable in the
- 45 circulation (<1 micromole), clinically significant drug-drug interactions due to inhibition of
- 46 P450-mediated metabolism EPA/DHA combinations are not expected in humans.

47 CLINICAL STUDIES

- 48 High Triglycerides: Add-on to HMG-CoA reductase inhibitor therapy: The effects of
- 49 LOVAZA 4 g per day as add-on therapy to treatment with simvastatin were evaluated in a
- 50 randomized, placebo-controlled, double-blind, parallel-group study of 254 adult patients (122 on
- 51 LOVAZA and 132 on placebo) with persistent high triglycerides (200 to 499 mg/dL) despite
- 52 simvastatin therapy (Table 1). Patients were treated with open-label simvastatin 40 mg per day
- 53 for 8 weeks prior to randomization to control their LDL-C to no greater than 10% above NCEP
- 54 ATP III goal and remained on this dose throughout the study. Following 8 weeks of open-label
- 55 treatment with simvastatin, patients were randomized to either LOVAZA 4 g per day or placebo
- 56 for an additional 8 weeks with simvastatin co-therapy. The median baseline triglyceride and
- 57 LDL-C levels in these patients were 268 mg/dL and 89 mg/dL, respectively. Median baseline
- 58 non-HDL-C and HDL-C levels were 138 mg/dL and 45 mg/dL, respectively.
- 59 The changes in the major lipoprotein lipid parameters for the groups receiving LOVAZA
- 60 plus simvastatin and placebo plus simvastatin are shown in Table 1.

61 Table 1. Response to the Addition of LOVAZA 4 g per day to On-going Simvastatin 40 mg

per aug 11	ior apj i			5	y corrac.		> ing/ all)	
	LOVAZA + Simvastatin N = 122			Placebo + Simvastatin N = 132			Difference	P-Value
Parameter								
	BL	ЕОТ	Median %	BL	ЕОТ	Median %		
			Change			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
Аро-В	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

62 per day Therapy in Patients With High Triglycerides (200 to 499 mg/dL)

63 BL = Baseline (mg/dL); EOT = End of Treatment (mg/dL); Median % Change = Median Percent

64 Change from Baseline; Difference = LOVAZA Median % Change – Placebo Median % Change

65

66 LOVAZA 4 g per day significantly reduced non-HDL-C, TG, TC, VLDL-C, and Apo-B

67 levels and increased HDL-C and LDL-C from baseline relative to placebo.

68 Very High Triglycerides: *Monotherapy:* The effects of LOVAZA 4 g per day were

69 assessed in 2 randomized, placebo-controlled, double-blind, parallel-group studies of 84 adult

70 patients (42 on LOVAZA, 42 on placebo) with very high triglyceride levels (Table 2). Patients

71 whose baseline triglyceride levels were between 500 and 2,000 mg/dL were enrolled in these 2

studies of 6 and 16 weeks' duration. The median triglyceride and LDL-C levels in these patients

73 were 792 mg/dL and 100 mg/dL, respectively. Median HDL-C level was 23.0 mg/dL.

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

76

Table 2. Median Baseline and Percent Change From Baseline in Lipid Parameters in Patients With Very High TG Levels (>500 mg/dL)

			0 /		
Parameter		/AZA = 42	Pla N =	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

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

80 Difference = LOVAZA Median % change – Placebo Median % Change

81

82 LOVAZA 4 g per day reduced median TG, VLDL-C, and non-HDL-C levels and increased

83 median HDL-C from baseline relative to placebo. Treatment with LOVAZA to reduce very high

- TG levels may result in elevations in LDL-C and non-HDL-C in some individuals. Patients
- should be monitored to ensure that the LDL-C level does not increase excessively.

- 86 The effect of LOVAZA on the risk of pancreatitis in patients with very high TG levels has
- 87 not been evaluated.
- 88 The effect of LOVAZA on cardiovascular mortality and morbidity in patients with elevated
- TG levels has not been determined.

90 INDICATIONS AND USAGE

- 91 **Very High Triglycerides:** LOVAZA is indicated as an adjunct to diet to reduce triglyceride 92 (*TG*) levels in adult patients with very high (\geq 500 mg/dL) triglyceride levels.
- 93 Usage Considerations: In individuals with hypertriglyceridemia (HTG), excess body weight
- 94 and excess alcohol intake may be important contributing factors and should be addressed before
- 95 initiating any drug therapy. Physical exercise can be an important ancillary measure. Diseases
- 96 contributory to hyperlipidemia, (such as hypothyroidism or diabetes mellitus) should be looked
 97 for and adequately treated. Estrogen therapy, thiazide diuretics, and beta blockers are sometimes
- 97 for and adequately freated. Estrogen merapy, mazide differences, and beta blockers are sometimes 98 associated with massive rises in plasma TG levels. In such cases, discontinuation of the specific
- etiologic agent, if medically indicated, may obviate the need for specific drug therapy for HTG.
- 100 The use of lipid-regulating agents should be considered only when reasonable attempts have
- been made to obtain satisfactory results with non-drug methods. If the decision is made to use

101 been made to obtain satisfactory results with hon-drug methods. If the decision is made to use

- 102 lipid-regulating agents, the patient should be advised that use of lipid-regulating agents does not
- 103 reduce the importance of adhering to diet (see PRECAUTIONS).

104 CONTRAINDICATIONS

LOVAZA is contraindicated in patients who exhibit hypersensitivity (e.g., anaphylacticreaction) to any component of this medication.

107 **PRECAUTIONS**

- 108 General: Initial Therapy: Laboratory studies should be performed to ascertain that the
- 109 patient's TG levels are consistently abnormal before instituting therapy with LOVAZA. Every
- 110 attempt should be made to control serum TG levels with appropriate diet, exercise, weight loss in
- 111 overweight patients, and control of any medical problems (such as diabetes mellitus and
- 112 hypothyroidism) that may be contributing to the patient's TG abnormalities. Medications known
- to exacerbate HTG (such as beta blockers, thiazides, and estrogens) should be discontinued or
- 114 changed, if possible, before considering TG–lowering drug therapy.
- 115 **Continued Therapy:** Laboratory studies should be performed periodically to measure the
- 116 patient's TG levels during therapy with LOVAZA. Therapy with LOVAZA should be withdrawn
- 117 in patients who do not have an adequate response after 2 months of treatment.
- 118 Information for Patients: LOVAZA should be used with caution in patients with known
- 119 sensitivity or allergy to fish.
- Patients should be advised that use of lipid-regulating agents does not reduce the importanceof adhering to diet.

122 Laboratory Tests: In some patients, increases in alanine aminotransferase (ALT) levels 123 without a concurrent increase in aspartate aminotransferase (AST) levels were observed. Alanine 124 aminotransferase levels should be monitored periodically during therapy with LOVAZA. 125 In some patients, LOVAZA increased low-density lipoprotein cholesterol (LDL-C) levels. As 126 with any lipid-regulating product, LDL-C levels should be monitored periodically during therapy with LOVAZA. 127 128 Drug Interactions: Anticoagulants: Some studies with omega-3-acids demonstrated 129 prolongation of bleeding time. The prolongation of bleeding time reported in these studies has 130 not exceeded normal limits and did not produce clinically significant bleeding episodes. Clinical 131 studies have not been done to thoroughly examine the effect of LOVAZA and concomitant 132 anticoagulants. Patients receiving treatment with both LOVAZA and anticoagulants should be 133 monitored periodically. 134 **HMG-CoA reductase inhibitors:** In a 14-day study of 24 healthy adult subjects, daily co-135 administration of simvastatin 80 mg with LOVAZA 4 g did not affect the extent (AUC) or rate 136 (C_{max}) of exposure to simvastatin or the major active metabolite, beta-hydroxy simvastatin at steady state. 137 138 Cytochrome P450-Dependent Monooxygenase Activities: Omega-3 fatty-acid-139 containing products have been shown to increase hepatic concentrations of cytochrome P450 and 140 activities of certain P450 enzymes in rats. The potential of LOVAZA to induce P450 activities in 141 humans has not been studied. 142 **Carcinogenesis**, **Mutagenesis**, **Impairment of Fertility**: In a rat carcinogenicity study with oral gavage doses of 100, 600, and 2,000 mg/kg/day, males were treated with omega-3-acid 143 144 ethyl esters for 101 weeks and females for 89 weeks without an increased incidence of tumors 145 (up to 5 times human systemic exposures following an oral dose of 4 g/day based on a body 146 surface area comparison). Standard lifetime carcinogenicity bioassays were not conducted in 147 mice. 148 Omega-3-acid ethyl esters were not mutagenic or clastogenic with or without metabolic 149 activation in the bacterial mutagenesis (Ames) test with Salmonella typhimurium and 150 Escherichia coli or in the chromosomal aberration assay in Chinese hamster V79 lung cells or 151 human lymphocytes. Omega-3-acid ethyl esters were negative in the in vivo mouse micronucleus 152 assay. 153 In a rat fertility study with oral gavage doses of 100, 600, and 2,000 mg/kg/day, males were 154 treated for 10 weeks prior to mating and females were treated for 2 weeks prior to and 155 throughout mating, gestation, and lactation. No adverse effect on fertility was observed at 2,000 156 mg/kg/day (5 times human systemic exposure following an oral dose of 4 g/day based on a body 157 surface area comparison). 158 Pregnancy Category C: There are no adequate and well-controlled studies in pregnant 159 women. It is unknown whether LOVAZA can cause fetal harm when administered to a pregnant 160 woman or can affect reproductive capacity. LOVAZA should be used during pregnancy only if 161 the potential benefit justifies the potential risk to the fetus.

162 Omega-3-acid ethyl esters have been shown to have an embryocidal effect in pregnant rats
163 when given in doses resulting in exposures 7 times the recommended human dose of 4 g/day
164 based on a body surface area comparison.

165 In female rats given oral gavage doses of 100, 600, and 2,000 mg/kg/day beginning 2 weeks 166 prior to mating and continuing through gestation and lactation, no adverse effects were observed

- in the high dose group (5 times human systemic exposure following an oral dose of 4 g/daybased on body surface area comparison).
- 169 In pregnant rats given oral gavage doses of 1,000, 3,000, and 6,000 mg/kg/day from gestation

day 6 through 15, no adverse effects were observed (14 times human systemic exposure
following an oral dose of 4 g/day based on a body surface area comparison).

172 In pregnant rats given oral gavage doses of 100, 600, and 2,000 mg/kg/day from gestation

173 day 14 through lactation day 21, no adverse effects were seen at 2,000 mg/kg/day (5 times the

174 human systemic exposure following an oral dose of 4 g/day based on a body surface area

175 comparison). However, decreased live births (20% reduction) and decreased survival to postnatal

176 day 4 (40% reduction) were observed in a dose-ranging study using higher doses of 3,000

- 177 mg/kg/day (7 times the human systemic exposure following an oral dose of 4 g/day based on a
- 178 body surface area comparison).
- 179 In pregnant rabbits given oral gavage doses of 375, 750, and 1,500 mg/kg/day from gestation
- 180 day 7 through 19, no findings were observed in the fetuses in groups given 375 mg/kg/day (2
- 181 times human systemic exposure following an oral dose of 4 g/day based on a body surface area
- 182 comparison). However, at higher doses, evidence of maternal toxicity was observed (4 times
- 183 human systemic exposure following an oral dose of 4 g/day based on a body surface area184 comparison).

185 **Nursing Mothers:** It is not known whether omega-3-acid ethyl esters are excreted in human

186 milk. Because many drugs are excreted in human milk, caution should be exercised when

187 LOVAZA is administered to a woman who is breastfeeding.

188 Pediatric Use: Safety and effectiveness in pediatric patients under 18 years of age have not
189 been established.

190 Geriatric Use: A limited number of patients older than 65 years were enrolled in the clinical

studies. Safety and efficacy findings in subjects older than 60 years did not appear to differ fromthose of subjects younger than 60 years.

ADVERSE REACTIONS

- 194 Treatment-emergent adverse events reported in at least 1% of patients treated with LOVAZA
- 195 4 g per day or placebo during 8 randomized, placebo-controlled, double-blind, parallel-group
- studies for HTG are listed in Table 3. Adverse events led to discontinuation of treatment in 3.5%
- 197 of patients treated with LOVAZA and 2.6% of patients treated with placebo.
- 198

199 Table 3. Adverse Events in Randomized, Placebo-Controlled, Double-Blind, Parallel-

200 Group Studies for Very High TG Levels (>500 mg/dL) That Used LOVAZA 4 g per Day

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

201 Adverse events were coded using COSTART, version 5.0. Subjects were counted only once for

202 each body system and for each preferred term.

203 * Placebo was corn oil for all studies.

204

Additional adverse events reported by 1 or more patients from 22 clinical studies for HTG are listed below:

Body as a Whole: Enlarged abdomen, asthenia, body odor, chest pain, chills, suicide, fever,
 generalized edema, fungal infection, malaise, neck pain, neoplasm, rheumatoid arthritis, and

209 sudden death.

210 Cardiovascular System: Arrhythmia, bypass surgery, cardiac arrest, hyperlipemia,

211 hypertension, migraine, myocardial infarct, myocardial ischemia, occlusion, peripheral vascular

212 disorder, syncope, and tachycardia.

213 **Digestive System:** Anorexia, constipation, dry mouth, dysphagia, colitis, fecal incontinence,

214 gastritis, gastroenteritis, gastrointestinal disorder, increased appetite, intestinal obstruction,

215 melena, pancreatitis, tenesmus, and vomiting.

- 216 Hematologic-Lymphatic System: Lymphadenopathy.
- 217 Infections and Infestations: Viral infection.

218 Metabolic and Nutritional Disorders: Edema, hyperglycemia, increased ALT, and

219 increased AST.

220 **Musculoskeletal System:** Arthralgia, arthritis, myalgia, pathological fracture, and tendon

disorder.

- 222 Nervous System: Central nervous system neoplasia, depression, dizziness, emotional lability,
- 223 facial paralysis, insomnia, vasodilatation, and vertigo.
- 224 **Respiratory System:** Asthma, bronchitis, increased cough, dyspnea, epistaxis, laryngitis,
- 225 pharyngitis, pneumonia, rhinitis, and sinusitis.
- 226 **Skin:** Alopecia, eczema, pruritus, and sweating.
- 227 **Special Senses:** Cataract.
- 228 Urogenital System: Cervix disorder, endometrial carcinoma, epididymitis, and impotence.
- 229 **Postmarketing Experience:** In addition to adverse reactions reported from clinical trials, the
- 230 events described below have been identified during post-approval use of LOVAZA. Because
- these events are reported voluntarily from a population of unknown size, it is not possible to
- reliably estimate their frequency or to always establish a causal relationship to drug exposure.
- 233 The following events have been reported: anaphylactic reaction, hemorrhagic diathesis.

234 DRUG ABUSE AND DEPENDENCE

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

236 **OVERDOSAGE**

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

239 DOSAGE AND ADMINISTRATION

- 240 Patients should be placed on an appropriate lipid-lowering diet before receiving LOVAZA,
- and should continue this diet during treatment with LOVAZA. In clinical studies, LOVAZA wasadministered with meals.
- The daily dose of LOVAZA is 4 g per day. The daily dose may be taken as a single 4-g dose (4 capsules) or as two 2-g doses (2 capsules given twice daily).

245 HOW SUPPLIED

- LOVAZA (omega-3-acid ethyl esters) capsules are supplied as 1-gram transparent soft-
- 247 gelatin capsules filled with light-yellow oil and bearing the designation REL900.
- 248 Bottles of 60: NDC 0173-0783-01
- 249 Bottles of 120: NDC 0173-0783-02
- 250 **Recommended Storage:** Store at 25°C (77°F); excursions permitted to 15°-30°C (59°-86°F)
- 251 [see USP Controlled Room Temperature]. Do not freeze. Keep out of reach of children.
- 252
- 253 Distributed by:

gsk GlaxoSmithKline

- 254
- 255 GlaxoSmithKline
- 256 Research Triangle Park, NC 27709

LVZ:3PI

257	
258	©2008 GlaxoSmithKline. All rights reserved
259	

260 November 2008

261

262	PHARMACIST-DETACH HERE AND GIVE INSTRUCTIONS TO PATIENT
263	
264	
265	PATIENT INFORMATION
266	LOVAZA [®] (lō-vā-ză)
267	(omega-3-acid ethyl esters) Capsules
268	
269	Read the Patient Information that comes with LOVAZA before you start taking it, and each time
270	you get a refill. There may be new information. This leaflet does not take the place of talking
271	with your doctor about your condition or treatment.
272	
273	What is LOVAZA?
274	LOVAZA is a prescription medicine for adults called a lipid-regulating medicine. LOVAZA is
275	made of omega-3 fatty acids. Omega-3 fatty acids are natural substances that your body needs.
276	They are found naturally in some plants and in the oil of certain fish, such as salmon and
277	mackerel
278	
279	LOVAZA is used along with a low-fat and low-cholesterol diet to lower very high triglycerides
280	(fats) in your blood. Before taking LOVAZA, talk to your healthcare provider about how you
281	can lower high blood fats by:
282	• losing weight, if you are overweight
283	increasing physical exercise
284	lowering alcohol use
285	• treating diseases such as diabetes and low thyroid (hypothyroidism)
286	• adjusting the dose or changing other medicines that raise triglyceride levels such as certain
287	blood pressure medicines and estrogens
288	Treatment with LOVATA has not been shown to provert heart attacks on stuckes
289	reatment with LOVAZA has not been snown to prevent heart attacks or strokes.
290	LOVAZA has not been studied in shildren under the age of 19 years
291	LOVAZA has not been studied in children under the age of 18 years.
292	Who should not take $I \cap V \wedge 7 \wedge ?$
293	$ \begin{array}{c} \text{Point take LOVAZA} \\ \text{De not take LOVAZA} \\ \text{if you:} \end{array} $
294 295	• are allergic to LOVAZA or any of its ingredients. See the end of this leaflet for a complete
296	list of ingredients in LOVAZA.
297	
298	What should I tell my doctor before taking LOVAZA?
299	Tell your doctor about all of your medical conditions, including if you:
300	 drink more than 2 glasses of alcohol daily
301	• have diabetes
302	have a thyroid problem called hypothyroidism
303	have a liver problem

304	have a pancreas problem
305	• are allergic to fish. LOVAZA may not be right for you.
306	• are pregnant, or planning to become pregnant. It is not known if LOVAZA can harm your
307	unborn baby.
308	• are breastfeeding. It is not known if LOVAZA passes into your milk and if it can harm your
309	baby.
310	
311	Tell your doctor about all the medicines you take, including prescription and non-prescription
312	medicine, vitamins and herbal supplements. LOVAZA and certain other medicines can interact
313	causing serious side effects. Especially tell your doctor if you take medicines:
314	• to reduce clotting – known as anticoagulants or blood thinners. These include aspirin
315	warfarin coumarin and clonidogral (PLAVIX)
216	warrann, countaint and ciopidogici (i EAVIA).
310 217	Know all the medicines you take. Know a list of them with you to show your destan and
317 210	Know all the medicines you take. Keep a list of them with you to show your doctor and
318	pharmacist.
319	
320	How should I take LOVAZA?
321	• Take LOVAZA exactly as prescribed. Do not change your dose or stop LOVAZA without
322	talking to your doctor.
323	• The usual dose of LOVAZA is 4 capsules:
324	• Take all 4 capsules at the same time, or
325	• Take 2 capsules two times a day
326	• Take LOVAZA at the same time or times each day.
327	• Take LOVAZA with or without food. You may find it easier to take LOVAZA with food.
328	• Do not take more than 4 capsules a day. Taking more than 4 capsules per day may increase
329	the chance of side effects.
33U 221	• Your doctor should start you on a low-fat and low-cholesterol diet before giving you
222	LOVAZA. Stay on this low-fat and low-choicesterol diet while taking LOVAZA.
333	• Four doctor should do blood tests to check your trigrycende and cholesteror levels, and liver function during treatment with LOVAZA
334	• If you miss a dose of LOVAZA take it as soon as you remember. However, if you miss one
335	day of LOVAZA, do not double your dose when you next take it.
336	• If you take too much LOVAZA or overdose, call your doctor or Poison Control Center right
337	away.
338	
339	What are the possible side effects of LOVAZA?
340	• The most common side effects with LOVAZA are burping, infection, flu symptoms, upset
341	stomach, a change in your sense of taste, back pain, and skin rash.
342	• LOVAZA may affect certain blood tests. It may change:
343	• one of the tests to check liver function (ALT)
344	• one of the tests to measure cholesterol levels (LDL-C)
345	
346	Talk to your doctor if you have side effects that bother you or that will not go away. You may
347	report side effects to FDA at 1-800-FDA-1088.
348	

- 349 These are not all the side effects with LOVAZA. Ask your doctor or pharmacist for a complete
- 350 list.
- 351

352 How should I store LOVAZA?

- Store LOVAZA at room temperature, 59° to 86° F (15° to 30° C). Do not freeze.
- Do not keep medicine that is out of date or that you no longer need.
- Keep LOVAZA out of the reach of children. Be sure that if you throw medicines away, it
 is out of the reach of children.
- 357

358 General information about LOVAZA

- 359 Medicines are sometimes prescribed for conditions that are not mentioned in patient information
- 360 leaflets. Do not use LOVAZA for a condition for which it was not prescribed. Do not give
- 361 LOVAZA to other people, even if they have the same problem you have. It may harm them.
- 362
- 363 This leaflet summarizes the most important information about LOVAZA. If you would like more
- information, talk with your doctor. You can ask your doctor or pharmacist for information about
- 365 LOVAZA that is written for health professionals or go to <u>www.LOVAZA.com</u>.
- 366

367 What are the ingredients in LOVAZA?

- 368 Active Ingredient: Omega-3-acid ethyl esters
- 369
- 370 Inactive Ingredients: Gelatin, glycerol, purified water, alpha-tocopherol (in partially
- 371 hydrogenated vegetable oils, including soybean oil)
- 372
- 373 LOVAZA is a registered trademark of the GlaxoSmithKline group of companies.
- 374 PLAVIX is a registered trademark of Sanofi-Synthelabo.
- 375
- 376 Distributed by:



- 377
- 378 GlaxoSmithKline
- 379 Research Triangle Park, NC 27709
- 380
- 381 ©2008 GlaxoSmithKline. All rights reserved.
- 382
- 383 June 2008

LVZ:1PIL