14 CLINICAL STUDIES

Clinical trials have not been conducted with LIPOFEN.

14.1 Primary Hypercholesterolemia (Heterozygous Familial and Nonfamilial) and Mixed Dyslipidemia

The effects of fenofibrate at a dose equivalent to 150 mg per day of LIPOFEN were assessed from four randomized, placebo-controlled, double-blind, parallel-group studies including patients with the following mean baseline lipid values: total-c 306.9 mg/dL; LDL-C 213.8 mg/dL; HDL-C 52.3 mg/dL; and triglycerides 191.0 mg/dL. Fenofibrate therapy lowered LDL-C, total-c, and the LDL-C/HDL-C ratio. Fenofibrate therapy also lowered triglycerides and raised HDL-C (see Table 4).

Table 4. Mean Percent Change in Lipid Parameters at End of Treatment[+]

Treatment Group	Total-C	LDL-C	HDL-C	TG
Pooled Cohort				
Mean baseline lipid values (n=646)	306.9 mg/dL	213.8 mg/dL	52.3 mg/dL	191.0 mg/dL
All FEN (n=361)	-18.7%*	-20.6%*	+11.0%*	* -28.9%*
Placebo (n=285)	-0.4%	-2.2%	+0.7%	+7.7%
Baseline LDL-C >160 mg/dL and TG <150 mg/dL				
Mean baseline lipid values (n=334)	307.7 mg/dL	227.7 mg/dL	58.1 mg/dL	101.7 mg/dL
All FEN (n=193)	-22.4%*	-31.4%*	+9.8%	-23.5%*
Placebo (n=141)	+0.2%	-2.2%	+2.6%	+11.7%
Baseline LDL-C >160 mg/dL and TG ≥150 mg/dL				
Mean baseline lipid values (n=242)	312.8 mg/dL	219.8 mg/dL	46.7 mg/dL	231.9 mg/dL
All FEN (n=126)	-16.8%*	-20.1%*	+14.6%*	-35.9%*
Placebo (n=116)	-3.0%	-6.6%	+2.3%	+0.9%

[+] Duration of study treatment was 3 to 6 months.
* p = <0.05 vs. Placebo

In a subset of the subjects, measurements of apo B were conducted. Fenofibrate treatment significantly reduced apo B from baseline to endpoint as compared with placebo (-25.1% vs. 2.4%, p<0.0001, n=213 and 143 respectively).

14.2 Severe Hypertriglyceridemia

The effects of fenofibrate on serum triglycerides were studied in two randomized, double-blind, placebo-controlled clinical trials of 147 hypertriglyceridemic patients. Patients were treated for eight weeks under protocols that differed only in that one entered patients with baseline TG levels of 500 to 1500 mg/dL, and the other TG levels of 350 to 500 mg/dL. In patients with hypertriglyceridemia and normal cholesterolemia with or without hyperchylomicronemia, treatment with fenofibrate at dosages equivalent to 150 mg LIPOFEN per day decreased primarily very low density lipoprotein (VLDL), triglycerides and VLDL cholesterol. Treatment of some with elevated triglycerides often results in an increase of LDL-C (see Table 5).

Table 5. Effects in Patients With Severe Hypertriglyceridemia

Study 1	Placebo				Fenofibrate			
Baseline TG Levels 350 to 499 mg/dL	N	Baseline (Mean)	Endpoint (Mean)	% Change (Mean)	N	Baseline (Mean)	Endpoint (Mean)	% Change (Mean)
Triglycerides	28	449	450	-0.5	27	432	223	-46.2*
VLDL Triglycerides	19	367	350	2.7	19	350	178	-44.1*
Total Cholesterol	28	255	261	2.8	27	252	227	-9.1*
HDL Cholesterol	28	35	36	4	27	34	40	19.6*
LDL Cholesterol	28	120	129	12	27	128	137	14.5
VLDL Cholesterol	27	99	99	5.8	27	92	46	-44.7*

Study 2	Placebo				Fenofibrate			
Baseline TG Levels 500 to 1500 mg/dL	N	Baseline (Mean)	Endpoint (Mean)	% Change (Mean)	N	Baseline (Mean)	Endpoint (Mean)	% Change (Mean)
Triglycerides	44	710	750	7.2	48	726	308	-54.5*
VLDL Triglycerides	29	537	571	18.7	33	543	205	-50.6*
Total Cholesterol	44	272	271	0.4	48	261	223	-13.8*
HDL Cholesterol	44	27	28	5.0	48	30	36	22.9*
LDL Cholesterol	42	100	90	-4.2	45	103	131	45.0*
VLDL Cholesterol	42	137	142	11.0	45	126	54	-49.4*

* = P<0.05 vs. Placebo

The effect of LIPOFEN on cardiovascular morbidity and mortality has not been determined.

16 HOW SUPPLIED/STORAGE AND HANDLING

LIPOFEN® (fenofibrate capsules, USP) is available in two strengths:

50 mg: Size 3 white opaque/white opaque gelatin capsule, imprinted in black ink with "50" between lines on the body, "G 246" on the cap and containing a white to almost white paste, available in bottles of 30 (NDC 66869-137-20) and 90 (NDC 66869-137-30).

150 mg: Size 1 white opaque/white opaque gelatin capsule, imprinted in green ink with "150" between lines on the body, "G 248" on the cap and containing a white to almost white paste, available in bottles of 30 (NDC 66869-147-20) and 90 (NDC 66869-147-30).

Store at 25ºC; Excursions permitted to 15ºC - 30ºC (59ºF - 86ºF). [See USP Controlled Room Temperature.] Keep out of the reach of children. Protect from moisture and light.

17 PATIENT COUNSELING INFORMATION

Patients should be advised:

- of the potential benefits and risks of LIPOFEN.
- not to use LIPOFEN if there is a known hypersensitivity to fenofibrate or fenofibric acid.
- of medications that should not be taken in combination with LIPOFEN.
- that if they are taking coumarin anticoagulants, LIPOFEN may increase their anti-coagulant effect, and increased monitoring may be necessary.
- to inform their physician of all medications, supplements, and herbal preparations they are taking and any change in their medical condition.
- to inform a physician prescribing a new medication, that they are taking LIPOFEN.
- to continue to follow an appropriate lipid-modifying diet while taking LIPOFEN.
- to take LIPOFEN once daily at the prescribed dose, swallowing each capsule whole.
- to inform their physician of any muscle pain, tenderness, or weakness; onset of abdominal pain; or any other new symptoms.
- not to breastfeed during treatment with LIPOFEN and for 5 days after the final dose.
- to return to their physician's office for routine monitoring.

Product of Israel

Manufactured for:
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