FENOFIBRATE

LIPWAY

160 mg Tablet

ANTIHYPERTRIGLYCERIDEMIA

FORMULATION
Each tablet contains:
Fenofibrate, USP ..... 160 mg

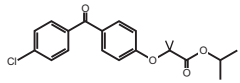
PRODUCT DESCRIPTION
Fenofibrate (Lipway) 160 mg is a white, caplet shaped, biconvex tablet, plain on both sides.

Chemical name: Isopropyl 2-[4-(4-chlorobenzoyl)phenoxy]-2-methylpropionate

Chemical formula: $C_{20}H_{21}ClO_4$

Molecular weight: 360.8

Chemical structure:



PHARMACODYNAMICS
Fenofibrate is a hypolipidaemic agent of the fibrate class, which inhibits the synthesis of cholesterol and triglycerides.

- Fenofibrate can lower blood cholesterol levels by 20 to 25% and blood triglyceride levels by 40 to 50%.
- The decrease in the cholesterol level is due to a reduction of the low density atherogenic fractions (VLDL and LDL). It improves the distribution of plasma cholesterol by reducing the total cholesterol: HDL cholesterol ratio, which increases in atherogenic hyperlipidaemia.
- A relationship has been established between hyperlipidaemia and atherosclerosis and between atherosclerosis and cardiovascular morbidity. Low HDL levels are associated with an increased risk of coronary disease. High triglyceride levels are associated with an increased vascular risk, but it has not been established that this relation is independent. Moreover, triglycerides may be involved in the process of atherogenesis and also of thrombogenesis.
- Extravascular deposits of cholesterol (xanthoma tendinosum and tuberosum) may regress considerably or even disappear completely with prolonged treatment.
- A Uricosuric effect has been demonstrated in hyperlipidaemic patients, with resultant mean reduction of blood uric acid of about 25%.
- With fenofibrate treatment, an increase in apoproteins A1 and a decrease in apoproteins B improve the apoprotein A1: apoprotein B ratio, which can be regarded as a marker of the risk of atherogenesis.
- An inhibitory effect of fenofibrate on platelet aggregation has been demonstrated in animals, and subsequently in man, in the course of clinical trial. It is manifested in reduction of aggregation induced by ADP, arachidonic acid and adrenaline.
- In rats treated with fenofibrate, 80% inhibition of hepatic microsomal HMG CoA activity has been observed. This phenomenon may explain the mechanism of action of fenofibrate in man.

The sustained release form makes it possible to maintain effective plasma concentrations for longer periods.

PHARMACOKINETICS

- Absorption
  The product is not found in unchanged form in the plasma. The major metabolite in the plasma is fenofibric acid. Fenofibric acid is strongly bound to plasma albumin and may displace oral anticoagulants from the protein binding sites and potentiate their anticoagulant effect.
  Fenofibrate is readily absorbed from the gastrointestinal tract when taken with food; absorption may be reduced if fenofibrate is given on an empty stomach.
- Plasma half-life
  Fenofibrate is rapidly hydrolysed to its active metabolite fenofibric acid which is about 99% bound to plasma albumin. The plasma elimination half-life of fenofibric acid is about 20 hours.
- Metabolism and excretion
  The product is eliminated essentially by the urinary route: 70% in 24 hours, 88% in 6 days, when the amount excreted attains 93% (urine and faeces). Fenofibrate is excreted principally as fenofibric acid and its glucuronide derivative. It is not removed by haemodialysis.

INDICATIONS
Adults Only
For the treatment of hyperlipidemias of type IIa, IIb, III, IV and V in patients who have not responded adequately to diet and other appropriate measures.

It is indispensable to continue the diet in all cases.
No long term controlled trials showing the efficacy of fenofibrate in the primary or secondary prevention of complications of atherosclerosis are available to date.

DOSAGE AND ADMINISTRATION
In combination with diet, this drug constitutes a long-term symptomatic treatment, the efficacy of which should be assessed regularly.
Adults:
For the management of primary hypercholesterolemia or mixed dyslipidemia: The recommended initial dosage of fenofibrate is 160 mg daily.
For the management of elevated serum triglyceride concentrations: The recommended initial dosage of fenofibrate in adults is 54-160 mg daily.

Dosage should be adjusted at intervals of 4-8 weeks until the desired effect on lipoprotein concentrations is observed or a maximum dosage of 160 mg daily.

Fenofibrate should be discontinued in patients who fail to achieve an adequate response after 2-3 months of therapy with the maximum recommended dosage of 160 mg daily.

Tablets should be swallowed whole during a meal.

Special Populations:
The recommended initial dosage of fenofibrate for the management of hyperlipoproteinemia in patients 65 years of age or older and in those with renal impairment (creatinine clearance less than 50 mL/minute) is 54 mg daily. Dosage should be adjusted only after evaluating therapeutic response and the effects of the drug on renal function.

CONTRAINDICATIONS
Absolute Contraindications
- Severe renal or hepatic impairment (see Warnings and Precautions)
- Existing gallbladder disease
- Pregnancy and breast feeding
- Photosensitivity
- Use in children

Relative Contraindications
- HMG CoA reductase inhibitors
- Other fibrates (see Interactions)

WARNINGS AND PRECAUTIONS
Warnings
- There have been report of muscle damage, including exceptional cases of rhabdomyolysis, with fibrates. This may occur more frequently in patients with hypoalbuminaemia.
- Muscle damage should be suspected in any patient who has diffuse myalgia, painful muscular sensitivity and/or major elevation of muscular CPK (5 times the normal level); in this situation the treatment should be discontinued.
- Moreover, the risk of muscle damage may be increased if the drug is administered in combination with another fibrate or with an HMG CoA reductase inhibitor (see Interactions).

Precautions
- If a satisfactory reduction of serum lipid concentrations has not been obtained after a period of administration of several months (3 to 6 months), additional or different therapeutic measures should be considered.
- Elevation, generally transient, of transaminase levels have been observed in some patients. On the basis of current knowledge, this would appear to justify the following measures:
  1. Liver function tests recommended every 3 months for the first year (discontinue treatment if significantly raised).
  2. Discontinuation of the treatment if ASAT and ALAT concentrations increase to over 3 times the upper normal limit.
  3. If the patient is receiving concomitant oral anticoagulant treatment, closer monitoring of prothrombin time, as expressed by the INR, is essential (see Interactions).

PREGNANCY AND LACTATION
Pregnancy
The results of animal studies have shown no evidence of teratogenic effect. In man, no malformations or foetotoxic effects have been observed to date. However, the experience of pregnancies exposed to fenofibrate is insufficient to rule out any risk. There is no indication of prescribing fibrates during pregnancy, with the exception of major hypertriglyceridaemia (>10g/L) insufficiently corrected by diet, which exposes the mother to the risk of acute pancreatitis.

Lactation
In the absence of information on the possible excretion of fenofibrate in breast milk, use of the product during lactation is not recommended.

EFFECTS ON THE ABILITY TO DRIVE AND USE MACHINES
Not applicable

INTERACTIONS
Inadvisable Combinations
- Other fibrates, HMG CoA reductase inhibitors: risk of additive undesirable muscular effects.

Combination requiring precautions
- Oral anticoagulants: increased effect of oral anticoagulants and greater risk of haemorrhage (through displacement of their plasma protein binding).

The INR should be monitored more frequently and the dosage of oral anticoagulants adjusted during and for 8 days after withdrawal of the treatment of with fenofibrate. The same of supervision is indispensable when switching to another fibrate, as the degree of potentiation is variable from one product to another.

ADVERSE DRUG REACTIONS
- Cases of muscle damage (diffuse myalgia, painful sensitivity, weakness) and exceptional cases of rhabdomyolysis, occasionally severe, have been reported as with other fibrates. They are generally reversible upon withdrawal of the treatment (see Special Warnings and Precautions).

Other undesirable effects of moderate intensity have also been reported infrequently:
- Digestive (gastric or intestinal) disorders of the dyspeptic type.
- Elevation of transaminase levels (see Warnings and Precautions)
- Hepatitis
- Photosensitivity
- Allergic skin reactions including rashes

In the absence of sufficiently long experience and of controlled clinical studies, it is not at present possible to make a general estimation of undesirable effects in the long term and more particularly of the risk of biliary lithiasis.

OVERDOSE AND TREATMENT
Symptomatic treatment

STORAGE CONDITION
Store at temperatures not exceeding 30ºC.

AVAILABILITY	REG. NO.	DATE OF 1st AUTHORIZATION
Fenofibrate (Lipway) 160 mg Tablet Alu/ Alu Strip Foil x 6's (Box of 30's)	DR-XY44257	19 March 2015

CAUTION
Foods, Drugs, Devices, and Cosmetics Act prohibits dispensing without prescription.

For suspected adverse drug reaction, report to the FDA: www.fda.gov.ph.
Seek advice from a healthcare professional at the first sign of any adverse drug reaction.

Marketing Authorization Holder
THE CATHAY DRUG CO., INC.
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Manufacturer
EL LABORATORIES, INC.
109 North Main Avenue, Laguna Technopark, Biñan, Laguna

Date of Revision: September 2019

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