FENOFIBRATE

LIPWAY SR

Sustained-Release Capsule

LIPID MODIFYING AGENT (FIBRATE)

℞

FORMULATION

Each sustained-release capsule contains:

Fenofibrate microgranules ..... 250 mg

PRODUCT DESCRIPTION

Fenofibrate (Lipway SR) 250 mg is a white to off-white spherical micogranules contained in EGC Size # 1, natural transparent capsule.

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 trigylceride 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 a resultant mean reduction of blood uric acid of about 25%.
- With fenofibrate treatment, an increase in apoproteins A1 and a decrease in apoproteins B imporve 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 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 gastroinstestinal 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. Fenofibric acid is not eliminated during haemodialysis.

INDICATIONS

Adults Only

For the treatment of hyperlipidaemias of types IIa, IIb, III, IV and V in patients who have not responded adequately to diet and other appropriate measures:

- If the blood cholesterol level remains high after dietary measures and/or associated risk factors exist.

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.

The average dosage is 1 sustained-release capsule of Lipway SR 250 mg per day.

CONTRAINDICATIONS

Absolute Contraindications

- Severe renal or hepatic impairment (see Warnings and Precautions for Use)
- Existing gall bladder disease
- Pregnancy and breastfeeding
- Photosensitivity
- In children

Relative Contraindications

- HMG-CoA reductase inhibitors
- Other fibrates (see interactions)

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 has been observed in some patients. On the basis of current knowledge, this would appear to justify the following measures:
  - Liver function tests recommended every 3 months for the first year (discontinue treatment if significantly raised)
  - Discontinuation of the treatment if ASAT and ALAT concentrations increase to over 3 times the upper normal limit.
- If the patient is receiving concomitant oral anticoagulant treatment, closer monitoring of prothrombin time, as expressed by the INR, is essential (see Interactions).

PREGNANCY

The results of animal studies have shown no evidence of a teratogenic effect. In man, no malformations or fetotoxic 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 hypertriglyceridemia (>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 the product during lactation is not recommended.

EFFECTS ON THE ABILITY TO DRIVE AND USE MACHINES

Not applicable

INTERACTIONS WITH OTHER PHARMACEUTICALS AND OTHER FORMS OF INTERACTION

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 hemorrhage (through displacement of their plasma protein binding).

The International Normalized Ratio (INR) should be monitored more frequently and the dosage of oral anticoagulants adjusted during and for 8 days after withdrawal of the treatment with fenofibrate. The same type 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 for Use).

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 for Use)
- 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

Fenofibrate cannot be eliminated by hydrolysis. If overdose is suspected, treat symptomatically and institute supportive measures as required.

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.

STORAGE

Store at temperatures not exceeding 30 °C.

AVAILABILITY	REG. NO.	DATE OF 1st AUTHORIZATION
Fenofibrate (Lipway SR) 250 mg Sustained-Release Capsule Blister pack x 10's (Box of 30's)	DR-XY28840	29 July 2003

Marketing Authorization Holder
THE CATHAY DRUG CO., INC.
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Manufacturer
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