FENOSUP® LIDOSE® 160 mg
Hard Capsule

1. NAME OF THE MEDICINAL PRODUCT
FENOSUP® LIDOSE® 160 mg, Hard Capsule

2.QUALITATIVE AND QUANTITATIVE COMPOSITION
Capsules containing Fenofibrate 160 mg.

3. PHARMACEUTICAL FORM
Hard capsule

4. CLINICAL PARTICULARS

4.1 Therapeutic indications
Hypercholesterolaemia and hypertriglyceridaemia alone or combined (types IIa, IIb, IV dyslipidaemias, as well as types III and V dyslipidaemias although only a few patients have been treated during clinical trials) in patients unresponsive to dietary and other non-drug therapeutic measures (e.g. weight reduction or increased physical activity), particularly when there is evidence of associated risk factors.
The treatment of secondary hyperlipoproteinaemias is indicated if the hyperlipoproteinaemia persists despite effective treatment of the underlying disease (e.g. dyslipidaemia in diabetes mellitus).
Dietary measures initiated before therapy should be continued.

4.2 Posology and method of administration

Posology

Adults: The recommended dose is one capsule containing 160 mg fenofibrate taken once daily.

Elderly patients: The usual adult dose is recommended.

Children: The use of the 160 mg dosage form is contraindicated in children.

If after several months of fenofibrate administration (e.g. 3 months) serum lipid levels have not been reduced satisfactorilly, complementary or different therapeutic measures should be considered.

Method of administration:
Capsule should be swallowed whole during a meal.

4.3 Contraindications
Hepatic insufficiency (including biliary cirrhosis), renal insufficiency, children, during pregnancy or lactation, hypersensitivity to fenofibrate or any component of this medication, known photoallergy or phototoxic reaction during treatment with fibrates or ketoprofen, gallbladder disease.

4,4 Special warnings and special precautions for use

Liver function:
As with other lowering agents, increases have been reported in transaminase levels in some patients. In the majority of cases these elevations were transient, minor and asymptomatic. It is recommended that transaminase levels be monitored every 3 months during the first 12 months of treatment. Attention should be paid to patients who develop

increase in transaminase levels and therapy should be discontinued if ASAT and ALAT levels increase to more than 3 times the upper limit of the normal range of 100 IU.

Muscle:
Muscle toxicity, including very rare cases of rhabdomyolysis, has been reported with administration of fibrates and other lipid-lowering agents. The incidence of this disorder increases in cases of hypoalbuminaemia and previous renal insufficiency. Muscle toxicity should be suspected in patients presenting diffuse myalgia, myositis, muscular cramps and weakness and/or marked increases in CPK (levels exceeding 5 times the normal range). In such cases treatment with fenofibrate should be stopped.

The risk of muscle toxicity may be increased if the drug is administered with another fibrate or an HMG-CoA reductase inhibitor, especially in cases of pre-existing muscular disease. Consequently, the co-prescription of fenofibrate with a statin should be reserve to patients with severe combined dyslipidaemia and high cardiovascular risk without any history of muscular disease. This combination therapy should be used with caution and patients should be monitored closely for signs of muscle toxicity.
For hyperlipidaemic patients taking oestragens or contraceptives containing oestrogen it should be ascertained whether the hyperlipidaemia is of primary or secondary nature (possible elevation of lipid values caused by oral oestrogen).

4.5 Interaction with other medicinal products and other forms of interaction

Oral anticoagulants:
Fenofibrate enhances oral anticoagulant effect and may increase risk of bleeding. It is recommended that the dose of anticoagulants is reduced by about one third at the start of treatment and then gradually adjusted if necessary according to INR (International Normalised Ratio) monitoring.

Cyclosporin:
Some severe cases of reversible renal function impairment have been reported during concomitant administration of fenofibrate and cyclosporin. The renal function of these patients must therefore be closely monitored and the treatment with fenofibrate stopped in the case of severe alteration of laboratory parameters.

HMG-CoA reductase inhibitors and other fibrates:

See section 4.4

Concurrent use of fibrates with HMG-CoA reductase inhibitors may cause severe myositis and myoglobinuria.

4.6 Pregnancy and lactation
Fenosup Lidose 160mg may not be used during pregnancy and lactation as no studies have been done during pregnancy and lactation in humans.

4.7 Effects on the ability to drive and use machines
No effect noted.

4.8 Undesirable effects
The most commonly reported adverse reactions:

Gastrointestinal: Digestive, gastric or intestinal disorders (abdominal pain, nausea, vomiting, diarrhoea, and flatulence) moderate in severity.

Skin: Reactions such as rashes, pruritus, urticaria or photosensitivity reactions, in individual cases (even after many months of uncomplicated use) cutaneous photosensitivity may occur with erythema, vesiculation or nodulation on parts of the skin exposed to sunlight or artificial UV light (e.g. sunlamp).

Less frequently reported adverse reactions:

Liver: Moderately elevated levels of serum transaminases may be found in some patients (see Special precautions for use). Episodes of hepatitis have been reported very rarely. When symptoms (e.g, jaundice, pruritus) indicative of hepatitis occur, laboratory tests are to be conducted for verification and fenofibrate discontinued, if applicable (see Special warnings).

Muscle: As with other lipid lowering agents, cases of muscle toxicity (diffuse myalgia, myositis, muscular cramps and weakness) and very rare cases of rhabdomyolysis have been reported. These effects are usually reversible when the drug is withdrawn (see Special warnings).

In rare cases, the following effects are reported:

Gallstones (but any causal relationship remains inconclusive), sexual asthenia and alopecia.
Increases in serum creatinine and urea, which are generally slight, and also a slight decrease in haemoglobin and leukocytes may be observed.

4.9 Overdose

No case of overdosage has been reported. No specific antidote is Known. If an overdose is suspected, treat symptomatically and institute appropriate supportive measures as required. Fenofibrate cannot be eliminated by haemodialysis.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Serum Lipid Reducing Agents / Cholesterol and Triglycerides Reducers / Fibrates.
ATC code: C10 AB 05
Fenofibrate is a fibric acid derivative whose lipid modifying effects reported in humans are mediated via activation of Peroxisome Proliferator Activated Receptor type alpha (PPARa),
Through activation of PPARa, fenofibrate increases the lipolysis and elimination of atherogenic triglyceride-rich particles from plasma by activating lipoprotein lipase and reducing production of apoprotein CIII. Activation of PPARa also induces an increase in the synthesis of apoproteins Al and All.
The above stated effects of fenofibrate on lipoproteins lead to a reduction in very low and low density fractions (VLDL and LDL) containing apoprotein B and an increase in the high density lipoprotein fraction (HDL) containing apoprotein Al and All.
In addition, through modulation of the synthesis and the catabolism of VLDL fractions fenofibrate increases the LDL clearance and reduces small dense LDL, the levels of which are elevated in the atherogenic

lipoprotein phenotype, a common disorder in patients at risk for coronary heart disease.
During clinical trials with fenofibrate, total cholesterol was reduced by 20 to 25%, triglycerides by 40 to 55% and HDL cholesterol was increased by 10 to 30%,
In hypercholesterolaemic patients, where LDL cholesterol levels are reduced by 20 to 35%, the overall effects on cholesterol results in a decrease in the ratios of total cholesterol to HDL cholesterol, LDL cholesterol to HDL cholesterol, or Apo Al, all of which are markers of atherogenic risk.
Because of its significant effect on LDL cholesterol and triglycerides, treatment with fenofibrate should be beneficial in hypercholesterolaemic patients with or without hypertriglyceridaemia, including secondary hyperlipoproteinaemia such as type 2 diabetes mellitus,
At the present time, no results of long-term controlled clinical trials are available to demonstrate the efficacy of fenofibrate in the primary or secondary prevention of atherosclerotic complications.
Extravascular deposits of cholesterol (tendinous and tuberous xanthoma) may be markedly reduced or even entirely eliminated fenofibrate therapy.
Patients with raised levels of fibrinogen treated with fenofibrate have shown significant reductions in this parameter, as have those with raised levels of Lp(a). Other inflammatory markers such as C-Reactive Protein are reduced with fenofibrate treatment.
The uricosuric effect of fenofibrate leading to reduction in uric acid levels of approximately 25 % should be of additional benefit in those dyslipidaemic patients with hyperuricaemia.
Fenofibrate has been shown to possess an anti-aggregatory effect on platelets in animals and in a clinical study, which showed a reduction in platelet aggregation induced by ADP, arachidonic acid and epinephrine.

5.2 Pharmacokinetic properties

FENOGAL 160 mg is a capsule containing 160 mg of fenofibrate and is suprabioavailable (larger bioavailability) compared to the previous formulations.

Absorption:
Maximum plasma concentrations (Cmax) occur within 4 to 5 hours after oral administration. Plasma concentrations are stable during continuous treatment in any given individual.

The absorption of fenofibrate is increased when administered with food.

Distribution:
Fenofibric acid is strongly bound to plasma albumin (more than 99%).

Plasma half-life:
The plasma elimination half-life of fenofibric acid is approximately 20 hours.

Metabolism and excretion:
No unchanged fenofibrate can be detected in the plasma where the principal metabolite is fenofibric acid. The drug is excreted mainly in the urine.

Practically all the drug is eliminated within 6 days. Fenofibrate is mainly excreted in the form of fenofibric acid and its glucuronide conjugate. In elderly patients, the fenofibric acid apparent total plasma clearance is not modified.

Kinetic studies following the administration of a single dose and continuous treatment have demonstrated that the drug does not accumulate. Fenofibric acid is not eliminated by haemodialysis.

5.3 Pre-clinical safety data
Chronic toxicity studies have yielded no relevant information about specific toxicity of fenofibrate.
Studies on mutagenicity of fenofibrate have been negative.
In rats and mice, liver tumours have been found at high dosages, which are attributable to peroxisome proliferation. These changes are specific to small rodents and have not been observed in other animal species. This is of no relevance to therapeutic use in man.
Studies in mice, rats and rabbits did not reveal any teratogenic effect. Embryotoxic effects were observed at doses in the range of maternal toxicity. Prolongation of the gestation period and difficulties during delivery were observed at high doses. No sign of any effect on fertility has been detected.

6. PHARMACEUTICAL PARTICULARS.

6.1 List of excipients
Lauroyl macrogolglycerides (Gelucire® 44/14), Macrogol 20.000 (PEG 20.000), Hydroxypropylcellulose (KLUCGEL XHF), Sodium starch glycolate (Explotab A)

6.2 Incompatibilities
Not applicable

6.3 Shelf life
3 years

6.4 Special precautions for storage
Store in the original package. Do not store above 30°C.

6.5 Nature and contents of container
Thermoformed blister strips (ALU/PVC).
Pack of 30 capsules.

6.6 Instructions for use and handling and disposal
Not applicable

7. DISTRIBUTED BY:

Pan-Malayan Pharmaceuticals Pte Ltd

For Hyphens Pharma Pte. Ltd.

8. MANUFACTURED BY:
SMB TECHNOLOGY S.A.
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9. DATE OF REVISION: August 2022