SUMMARY OF PRODUCT CHARACTERISTICS

1. Name of the medicinal product:
LIPILOC 10 RZ
(Rosuvastatin 10 mg and Fenofibrate 160 mg Tablets)

2. Qualitative and quantitative composition
LIPILOC 10 RZ (Rosuvastatin 10 mg and Fenofibrate 160 mg Tablets)
Each film coated tablets contains:
Rosuvastatin Calcium equivalent to Rosuvastatin 10 mg
Fenofibrate BP 160 mg
Excipients q.s.
Colour: Iron oxide yellow, Titanium Dioxide BP
For the full list of excipients, see section 6.1.

3. Pharmaceutical form
Film-coated Tablets
Description: Yellow, circular shaped, biconvex, film coated tablet, plain on both sides.

4. Clinical particulars
4.1 Therapeutic indications Mixed Dyslipidemia
Lipiloc 10 RZ is indicated as adjunctive therapy to diet to reduce elevated total-C, LDL-C, ApoB, and triglycerides and to increase HDL-C in adult patients with mixed dyslipidemia (Fredrickson Types II a and II b).

Hypercholesterolemia
Lipiloc 10 RZ is indicated as adjunctive therapy to diet to reduce elevated total-C, LDL-C, ApoB, and to increase HDL-C in adult patients with primary hypercholesterolemia

Hypertriglyceridemia
Lipiloc 10 RZ is indicated as adjunctive therapy to diet for the treatment of adult patients with hypertriglyceridemia (Fredrickson Types IV and V hyperlipidemia).

Lipid-altering agents should be used in addition to a diet restricted in saturated fat and cholesterol when response to diet and non-pharmacological interventions alone has been inadequate. (See National Cholesterol Education Program Treatment Guidelines, summarized in Table 1 below).

Table 1: NCEP guidelines for lipid management

Risk category	LDL goal (mg/dL)	LDL level at which to consider drug therapy (mg/dL)
CHD *or CHD risk equivalents (10-year risk >20%)	<100	≥130(100-129: drug optional)
2+ Risk Factors (10-year risk ≤20%)	<130	10-year risk 10%-20%: ≥130 10-year risk <10%: ≥160
0-1 Risk Factor **	<160	(160-189: LDL-lowering drug optional)

*CHD = coronary heart disease

**Almost all people with 0-1 risk factor have 10-year risk <10%; thus, 10-year risk assessment in people with 0-1 risk factor is not necessary.

After the LDL-C goal has been achieved, if the TG is still ≥200 mg/dL, non HDL-C (total-C minus HDL-C) becomes a secondary target of therapy. Non-HDL-C goals are set 30 mg/dL higher than LDL-C goals for each risk category

4.2 Posology and method of administration
Patients should be placed on an appropriate lipid-lowering diet before receiving Lipiloc 10 RZ, and should continue this diet during treatment. The recommended dosage is one tablet once daily

Dosing in Patients with Renal Impairment
Fenofibrate should be initiated at a lower dose in patients having mild to moderately impaired renal function and it should be avoided in patients with severe renal impairment. As Lipiloc 10 RZ contains 160mg of FenoFibrate, it should be avoided in all renal impairment patients.

Dosage in Asian Patients
In Asian patients, consider initiation of Lipiloc 10 RZ therapy with 5mg once daily due to increased Rosuvastatin plasma concentrations. The increased systemic exposure should be taken into consideration when treating Asian patients not adequately controlled at doses up to 20mg/day.

Use with Concomitant Therapy Patients taking Cyclosporine
The dose of Lipiloc 10 RZ should not exceed 5mg once daily

Patients Taking Gemfibrozil
Initiate Lipiloc 10 RZ therapy with 5 mg once daily. The dose of Lipiloc 10 RZ should not exceed 10mg once daily.

Patients Taking Lopinavir and Ritonavir or Atazanavir and Ritonavir
Initiate Lipiloc 10 RZ therapy with 5 mg once daily. The dose of Lipiloc 10 RZ should not exceed 10mg once daily

4.3 Contraindications
This combination is contra indicated in:
- Patients who are hypersensitivity to any component of this product
- Patients with active liver disease or renal impairment.
- Patients with preexisting gall bladder disease
- Pregnancy and lactation.

4.4 Special warnings and precautions for use Liver Dysfunction:
It is recommended that liver enzyme tests be performed before the initiation of rosuvastatin, and if signs or symptoms of liver injury occur. Increases in serum transaminases [AST (SGOT) or ALT (SGPT)] have been reported with HMG- CoA reductase inhibitors, including rosuvastatin. In most cases, the elevations were transient and resolved or improved on continued therapy or after a brief interruption in therapy. There were two cases of jaundice, for which a relationship to rosuvastatin therapy could not be determined, which resolved after discontinuation of therapy. There were no cases of liver failure or irreversible liver disease in these trials. In a pooled analysis of placebo-controlled trials, increases in serum transaminases to greater than 3 times the upper limit of normal occurred in 1.1% of patients taking rosuvastatin versus 0.5% of patients treated with placebo. There have been rare postmarketing reports of fatal and non-fatal hepatic failure in patients taking statins, including rosuvastatin. If serious liver injury with clinical symptoms and/or hyperbilirubinemia or jaundice occurs during treatment with rosuvastatin, promptly interrupt therapy. If an alternate etiology is not found, do not restart rosuvastatin.
Rosuvastatin should be used with caution in patients who consume substantial quantities of alcohol and/or have a history of chronic liver disease. Active liver disease, which may include unexplained persistent transaminase elevations, is a contraindication to the use of rosuvastatin.

Hepatic insufficiency:
In a study in subjects with varying degrees of hepatic impairment there was no evidence of increased exposure to Rosuvastatin other than in the 2 subjects with the most severe liver disease (Child-Pugh scores of

8 and 9). In these subjects systemic exposure was increased by at least 2-fold compared with subjects with lower Child-Pugh scores. Its recommended that the liver enzyme tests be performed before and after 12 weeks following both the initiation of therapy and any elevation of dose thereafter.

Renal effects:
An assessment of renal function should be considered during routine follow-up of patients treated with higher dose.

Skeletal muscle:
Effects on skeletal muscle e.g. uncomplicated myalgia, myopathy and rhabdomyolysis, have been reported in patients treated with Rosuvastatin. Patients who develop any signs or symptoms suggestive of myopathy should have their CK levels measured. Rosuvastatin therapy should be discontinued if myopathy is diagnosed or suspected. An increase in the incidence of myositis and myopathy has been seen in patients receiving other HMG-CoA reductase inhibitors together with cyclosporin, fibric acid derivatives, including gemfibrozil, nicotinic acid, azole antifungals and macrolide antibiotics. Rosuvastatin should be prescribed with caution in patients with pre-disposing factors for myopathy, such as renal impairment, advanced age and hypothyroidism, or situations where an increase in plasma levels may occur. Rosuvastatin should be temporarily with held in any patient with an acute serious condition suggestive of myopathy or predisposing to the development of renal failure secondary to rhabdomyolysis (e.g. sepsis, hypotension, major surgery, trauma, severe metabolic, endocrine and electrolyte disorders; or uncontrolled seizures).
Fenofibrate: Adverse events reported by 2% or more of patients treated with Fenofibrate during the double-blind, placebo-controlled trials, regardless of causality, are listed in the table below. Adverse events led to discontinuation of treatment in 5% of patients treated with Fenofibrate and in 3% treated with placebo. Increases in liver function tests were the most frequent events, causing discontinuation of Fenofibrate treatment in 1.6% of patients in double-blind trials. There is no specific treatment in the event of overdose. In the event of overdose, the patient should be treated symptomatically and supportive measures instituted as required. If indicated, elimination of unabsorbed drug should be achieved by emesis or gastric lavage; usual precautions should be observed to maintain the airway. Hemodialysis is unlikely to be of benefit.

4.5 Interaction with other medicinal products and other forms of interaction Rosuvastatin:
Interaction with other medicinal products and other forms of interaction:

- Cyclosporin: Rosuvastatin steady state $AUC_{(0-t)}$ increased up to 7-fold over that seen in healthy volunteers administered the same dose.
- Gemfibrozil: Concomitant use of Rosuvastatin and gemfibrozil resulted in a 2-fold increase in Rosuvastatin C_{max} and $AUC_{(0-t)}$.

- Protease Inhibitor: Coadministration of Rosuvastatin with certain protease inhibitors given in combination with ritonavir has different effects on rosuvastatin exposure. The protease inhibitor combinations lopinavir/ritonavir and atazanavir/ritonavir increase Rosuvastatin exposure upto threefold. For these combination the dose of Rosuvastatin is restricted to low dose.
- Coumarin Anticoagulants: Rosuvastatin significantly increased INR (International Normalized Ratio) in patients receiving coumarin anticoagulants. Therefore caution should be excercised when coumarin anticoagulants are given in conjunction with Rosuvastatin. In patients taking coumarin anticoagulants and Rosuvastatin concomitantly INR should be determined before starting Rosuvastatin and frequently enough during early therapy to ensure that no significant alteration of INR occurs.
- Niacin: The skeletal muscle effects may be enhanced with Rosuvastatin in used with combination Niacin; a reduction in Rosuvastatin dosage should be considered.

Fenofibrate:

- Oral Anticoagulants: Caution should be exercised when coumarin anticoagulants are given along with fenofibrate. The dosage of anticoagulant should be reduced to maintain the prothrombin time/INR.
- Cyclosporine: Because cyclosporine can produce nephrotoxicity with decreases in creatinine clearance and rises in serum creatinine and because renal excretion is the primary elimination route of fibrate drugs including Fenofibrate, there is a risk that an interaction will lead to deterioration.

4.6 Fertility, Pregnancy and lactation
The safety of this combination, during pregnancy and breast-feeding has not been established. Women of childbearing potential should use appropriate contraceptive measures and seek advice from their physician.

4.7 Effects on ability to drive and use machines
Not applicable

4.8 Undesirable effects:
Rosuvastatin is generally well tolerated. The adverse events seen with Rosuvastatin are generally mild and transient. In controlled clinical trials less than 4% of Rosuvastatin treated patients were withdrawn due to adverse events. The frequencies of adverse events are ranked according to the following: Common (> 1/100, < 1/10); Uncommon (> 1/1000, < 1/100); Rare (> 1/10 000, < 1/1000).
Nervous system disorders:
Common: headache, dizziness and memory loss Gastrointestinal disorders: Common: constipation, nausea, abdominal pain Musculoskeletal, connective tissue and bone disorders: Common: myalgia Rare: myopathy, rhabdomyolysis General disorders: Common: asthenia Skin disorders: Uncommon: pruritis, rash, urticaria Rare: hypersensitivity reactions including angiooedema. The incidence of adverse drug reactions tends to increase with increasing dose.

Skeletal muscle effects:
Rhabdomyolysis, which may occasionally be associated with impairment of renal function, has been reported with Rosuvastatin. Renal effects: Proteinuria Laboratory effects: A dose-related increase in liver transaminases and CK has been observed in patients taking Rosuvastatin. Abnormal urinalysis testing (dipstick-positive proteinuria with haematuria) has been seen in patients taking Rosuvastatin. The protein detected was mostly tubular in origin. In most cases, proteinuria decreases or disappears spontaneously on reduction of dose.

Risk of Hyperglycemia:
Increase in blood sugar levels (hyperglycemia) have been reported with rosuvastatin.

Reporting of suspected adverse reactions:
Reporting suspected adverse reactions after authorization of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are requested to report any suspected adverse reactions via pharmacy and poisons board, Pharmacovigilance Electronic Reporting System (PvERS) https://pv.pharmacyboardkenya.org.

4.9 Overdose
General supportive care of the patient is indicated, including monitoring of vital signs and observation of clinical status, should an overdose occur. If indicated, elimination of unabsorbed drug should be achieved by emesis or gastric lavage;usual precautions should be observed to maintain the airway. Due to extensive drug binding to plasma proteins, hemodialysis should not be considered.

5. Pharmacological properties
5.1 Pharmacodynamic properties

Rosuvastatin
Rosuvastatin is a selective and competitive inhibitor of 3-hydroxy-3-methylglutaryl coenzyme A (HMG- CoA) reductase, the rate-limiting enzyme that converts HMG-CoA to mevalonate, a precursor of cholesterol. In vivo studies in animals and in vitro studies in cultured animal and human cells have shown rosuvastatin to have a high uptake into, and selectivity for, action in the liver, the target organ for cholesterol lowering. In in vivo and in vitro studies, rosuvastatin produces its lipid-modifying effects in

two ways. First, it increases the number of hepatic low-density lipoprotein (LDL) receptors on the cell- surface to enhance uptake and catabolism of LDL. Second, rosuvastatin inhibits hepatic synthesis of very low-density lipoprotein (VLDL), which reduces the total number of VLDL and LDL particles.

Fenofibrate
The active moiety is fenofibric acid. The pharmacological effects of fenofibric acid in both animals and humans have been extensively studied through oral administration of fenofibrate.
The lipid-modifying effects of fenofibric acid seen in clinical practice have been explained in vivo in transgenic mice and in vitro in human hepatocyte cultures by the activation of peroxisome proliferator activated receptor-alpha (PPAR-alpha). Through this mechanism, fenofibrate increases lipolysis and elimination of triglyceride (TG)-rich particles from plasma by activating lipoprotein lipase and reducing production of apoprotein C-III (an inhibitor of lipoprotein lipase activity).
The resulting decrease in TG produces an alteration in the size and composition of LDL from small, dense particles (which are thought to be atherogenic due to their susceptibility to oxidation), to large buoyant particles. These larger particles have a greater affinity for cholesterol receptors and are catabolized rapidly. Activation of PPAR-alpha also induces an increase in the synthesis of apolipoproteins A-I, A-II and high- density lipoprotein cholesterol (HDL-C).
Fenofibrate also reduces serum uric acid levels in hyperuricemic and normal individuals by increasing the urinary excretion of uric acid.
A variety of clinical studies have demonstrated that elevated levels of total cholesterol (total-C), LDL cholesterol (LDL-C), and apolipoprotein B (apo B), an LDL membrane complex, are associated with human atherosclerosis. Similarly, decreased levels of HDL-C and its transport complex, apolipoprotein A (apo AI and apo AII) are associated with the development of atherosclerosis. Epidemiologic investigations have established that cardiovascular morbidity and mortality vary directly with the level of total-C, LDL-C, and TG, and inversely with the level of HDL-C. The independent effect of raising HDL-C or lowering TG on the risk of cardiovascular morbidity and mortality has not been determined.
Fenofibric acid, the active metabolite of fenofibrate, produces reductions in total-C, LDL-C, apo B, total TG and TG rich lipoprotein (VLDL) in treated patients. In addition, treatment with fenofibrate results in increases in HDL-C and apolipoproteins apoAI and apoAII.

5.2 Pharmacokinetic properties

In clinical pharmacology studies in man, peak plasma concentrations of rosuvastatin were reached 3 to 5 hours following oral dosing. Both peak concentration (C max) and area under the plasma concentration-time curve (AUC) increased in approximate proportion to rosuvastatin dose. The absolute bioavailability of rosuvastatin is approximately 20%. Administration of rosuvastatin with food did not affect the AUC of rosuvastatin. The AUC of rosuvastatin does not differ following evening or morning drug administration.
Plasma concentrations of fenofibric acid after administration of one 145 mg tablet are equivalent under fed conditions to one 200 mg micronized fenofibrate capsule. Fenofibrate is a pro-drug of the active chemical moiety fenofibric acid. Fenofibrate is converted by ester hydrolysis in the body of fenofibric acid, which is the active constituent measurable in the circulation. The absolute bioavailability of fenofibrate cannot be determined as the compound is virtually insoluble in aqueous media suitable for injection. However, fenofibrate is well absorbed from the gastrointestinal tract. Following oral administration in healthy volunteers, approximately 60% of a single dose of radio labeled fenofibrate appeared

in urine, primarily as fenofibric acid and its glucuronate conjugate, and 25% was excreted in the feces. Peak plasma levels of fenofibric acid occur within 6 to 8 hours after administration. Exposure to fenofibric acid in plasma, as measured by C max and AUC, is not significantly different when a single 145 mg dose of fenofibrate is administered under fasting or non fasting conditions.

Distribution
Mean volume of distribution at steady-state of rosuvastatin is approximately 134 liters.Rosuvastatin is 88% bound to plasma proteins, mostly albumin. This binding is reversible and independent of plasma concentrations.
Upon multiple dosing of fenofibrate, fenofibric acid steady state is achieved within 9 days. Plasma concentrations of fenofibric acid at steady state are approximately double of those following a single dose. Serum protein binding was approximately 99% in normal and hyperlipidemic subjects.

Metabolism
Rosuvastatin is not extensively metabolized; approximately 10% of a radiolabeled dose is recovered as metabolite. The major metabolite is N-desmethyl rosuvastatin, which is formed principally by cytochrome (CY) P450 2C9, and in vitro studies have demonstrated that N-desmethyl rosuvastatin has approximately one-sixth to one-half the HMG-CoA reductase inhibitory activity of the parent compound. Overall, greater than 90% of active plasma HMG-CoA reductase inhibitory activity is accounted for by the parent compound.
Following oral administration, fenofibrate is rapidly hydrolyzed by esterases to the active metabolite, fenofibric acid; no unchanged fenofibrate is detected in plasma. Fenofibric acid is primarily conjugated with glucuronic acid and then excreted in the urine. A small amount of fenofibric acid is reduced at the carbonyl moiety to a benzhydrol metabolite which is, in turn, conjugated with glucuronic acid and excreted in urine. In vivo metabolism data indicate that neither fenofibrate nor fenofibric acid undergo oxidative metabolism (e.g., CYP450) to a significant extent.
Excretion
Following oral administration, rosuvastatin and its metabolites are primarily excreted in the feces (90%). The elimination half-life (t 1/2) of rosuvastatin is approximately 19 hours. After an intravenous dose, approximately 28% of total body clearance was via the renal route, and 72% by the hepatic route.
After absorption, fenofibrate is mainly excreted in the urine in the form of metabolites, primarily fenofibric acid and fenofibric acid glucuronide. After administration of radio labeled fenofibrate, approximately 60% of the dose appeared in the urine and 25% was excreted in the feces. Fenofibric acid is eliminated with a half-life of 20 hours, allowing once daily dosing.

Special Population
Geriatric: There were no differences in plasma concentrations of rosuvastatin between the non-elderly and elderly populations (age >65 years).
In elderly volunteers, 77 to 87 years of age, the oral clearance of fenofibric acid following a single oral dose of fenofibrate was 1.2 L/h, which compares to 1.1 L/h in young adults. This indicates that a similar dosage regimen can be used in elderly with normal renal function, without increasing accumulation of the drug or metabolites.

Pediatric: The pharmacokinetics of fenofibrate has not been studied in pediatric populations.

Gender: No pharmacokinetic difference between males and females has been observed for rosuvastatin or fenofibrate.

Renal Impairment: Mild to moderate renal impairment had no influence on plasma concentrations of rosuvastatin. However, plasma concentrations of rosuvastatin increased to a clinically significant extent (about 3-fold) in patients with severe renal impairment (CL cr<30 mL/min/1.73 m 2) not receiving hemodialysis compared with healthy subjects (CL cr>80 mL/min/1.73 m 2).
The pharmacokinetics of fenofibric acid was examined in patients with mild, moderate, and severe renal impairment. Patients with severe renal impairment (estimated glomerular filtration rate <30 mL/min/1.73 m 2) showed 2.7-fold increase in exposure for fenofibric acid and increased accumulation of fenofibric acid during chronic dosing compared to that of healthy subjects. Patients with mild-to-moderate renal impairment (eGFR 30-59 mL/min/1.73 m 2) had similar exposure but an increase in the half- life for fenofibric acid compared to that of healthy subjects. Based on these findings, the use of FENOFIBRATE 145 MG AND ROSUVASTATIN 5 MG TABLET should be avoided in patients who have severe renal impairment and dose reduction is required in patients having mild-to-moderate renal impairment.
Hemodialysis: Steady-state plasma concentrations of rosuvastatin in patients on chronic hemodialysis were approximately 50% greater compared with healthy volunteer subjects with normal renal function.
Hepatic Impairment: In patients with chronic alcohol liver disease, plasma concentrations of rosuvastatin were modestly increased. In patients with Child-Pugh A disease, C max and AUC were increased by 60% and 5%, respectively, as compared with patients with normal liver function. In patients with Child-Pugh B disease, C max and AUC were increased 100% and 21%, respectively, compared with patients with normal liver function.
No pharmacokinetic studies have been conducted with fenofibrate in patients having hepatic insufficiency. Race: A population pharmacokinetic analysis revealed no clinically relevant differences in pharmacokinetics among Caucasian, Hispanic and Black or Afro-Caribbean groups,However, pharmacokinetic studies have demonstrated an approximate 2-fold elevation in median exposure (AUC and C max) in Asian subjects when compared with a Caucasian control group.
The influence of race on the pharmacokinetics of fenofibrate has not been studied; however, fenofibrate is not metabolized by enzymes known for exhibiting inter-ethnic variability

5.3 Preclinical safety data
Rosuvastatin:
Preclinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, genotoxicity and carcinogenicity potential. Specific tests for effects on hERG have not been evaluated. Adverse reactions not observed in clinical studies, but seen in animals at exposure levels similar to clinical exposure levels were as follows: in repeated-dose toxicity studies histopathologic liver changes likely due to the pharmacologic action of rosuvastatin were observed in mouse, rat, and to a lesser extent with effects in the gall bladder in dogs, but not in monkeys. In addition, testicular toxicity was observed in monkeys and dogs at higher dosages. Reproductive toxicity was evident in rats, with reduced litter sizes, litter weight and pup survival observed at maternally toxic doses, where systemic exposures were several times above the therapeutic exposure level.

Fenofibrate:
Chronic toxicity studies have yielded no relevant information about specific toxicity of fenofibrate. Studies on the 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

Microcrystalline Cellulose (pH 102), Sodium Lauryl Sulphate, Crospovidone XL 10, Croscarmellose Sodium, Pregelatinised Starch, Povidone (P.V.P.K 30), Isopropyl Alcohol, Colloidal Anhydrous Silica, Magnesium Stearate, Hypromellose (E-15), Macrogols (PEG 6000), Titanium Dioxide, Purified Talc, Iron Oxide yellow, Methylene Chloride.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

36 months

6.4 Special precautions for storage

Store at a temperature below 30^0C protected from light and moisture. Keep out of reach of children

6.5 Nature and contents of container

Alu-Alu Blister pack of 3 x 10 Tablets

6.6 Special precautions for disposal and other handling

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. Marketing Authorisation Holder &Manufacturing Site Addresses

MARKETING AUTHORISATION HOLDER (MAH):
GALAXY PHARMACEUTICAL LTD. P.O. BOX 39107-00623, NAIROBI, KENYA.

MANUFACTURER:
FREDUN PHARMACEUTICALS LTD
14,15,16. Zorabian industrial Complex Veoor Palghar (E) – 401404. India

8. Marketing authorisation number (s)

CTD11444

9. Date of first authorisation/renewal of the authorisation

29/07/2026

10. Date of revision of the text
29/07/2026