Prescribing Information For the use of Registered Medical Practitioner or Hospital or Laboratory Only.

FENO-TG 160 MG TABLETS

Fenofibrate Tablets

COMPOSITION :
Each film coated tablet contains :
Fenofibrate BP 160 mg.

DESCRIPTION :
FENO-TG 160 mg Tablets (Fenofibrate Tablets), is a lipid regulating agent available as tablets for oral administration.
Orange coloured, round shape, biconvex film coated tablets.

CLINICAL PHARMACOLOGY :
Elevated levels of total cholesterol (total-C), low density lipoprotein cholesterol (LDL-C), and apolipoprotein B (apo B), an LDL membrane complex, are associated with human atherosclerosis. Similarly, decreased levels of high density lipoprotein cholesterol (HDL-C) and its transport complex, apolipoprotein A (apo AI and apo AII) are associated with the development of atherosclerosis.
Fenofibric acid, the active metabolite of fenofibrate, produces reductions in total cholesterol, LDL cholesterol, apolipoprotein B, total triglycerides and triglyceride rich lipoprotein (VLDL). In addition, treatment with fenofibrate results in increases in high density lipoprotein (HDL) and apoproteins apoAI and apoAII.
The effects of fenofibric acid have been explained by the activation of peroxisome proliferator activated receptor α (PPAR α). Through this mechanism, fenofibrate increases lipolysis and elimination of triglyceride-rich particles from plasma by activating lipoprotein lipase and reducing production of apoprotein C-III (an inhibitor of lipoprotein lipase activity). The resulting fall in triglycerides 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 α also induces an increase in the synthesis of apoproteins A-I, A-II and HDL-cholesterol.
Fenofibrate also reduces serum uric acid levels in hyperuricemic and normal individuals by increasing the urinary excretion of uric acid.
Pharmacokinetics/ Metabolism :
Absorption : Fenofibrate is well absorbed from the gastrointestinal tract. Following oral administration, approximately 60% of a single dose of radiolabelled 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.
Distribution : Steady-state plasma levels of fenofibric acid were shown to be achieved within 5 days of dosing and did not demonstrate accumulation across time following multiple dose administration. Serum protein binding was approximately 99% in normal and hyperlipidemic subjects.
Metabolism : 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 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.
Neither fenofibrate nor fenofibric acid undergo oxidative metabolism (e.g.,cytochrome P450) to a significant extent.
Excretion : After absorption, fenofibrate is mainly excreted in the urine in the form of metabolites, primarily fenofibric acid and fenofibric acid glucuronide. Fenofibric acid is eliminated with a half-life of 20 hours, allowing once daily administration in a clinical setting.

INDICATIONS AND USAGE :
Hypercholesterolaemia and hypertriglyceridaemia alone or combined (types IIa, IIb, III, IV and V dyslipidaemias) 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.

DOSAGE AND ADMINISTRATION :
The recommended dose of **FENO-TG** 160 mg Tablets is one tablet taken once daily. Tablets should be swallowed during a meal with water. The usual adult dose is recommended in elderly patients. In renal dysfunction, the dosage may need to be reduced depending on the rate of creatinine clearance.

CONTRAINDICATIONS :
FENO-TG 160 mg Tablets is contraindicated in patients who exhibit hypersensitivity to fenofibrate.
FENO-TG 160 mg Tablets is contraindicated in patients with hepatic or severe renal dysfunction, including primary biliary cirrhosis, and patients with unexplained persistent liver function abnormality.
FENO-TG 160 mg Tablets is contraindicated in patients with preexisting gallbladder disease. Also contraindicated in children. Known photoallergy or phototoxic reactions during treatment with fibrates or ketoprofen.

WARNINGS :
Liver Function :
Fenofibrate has been associated with increases in serum transaminases [AST (SGOT) or ALT (SGPT)]. Increases to > 3 times the upper limit of normal occurred in 5.3% of patients taking fenofibrate.
The incidence of increases in transaminases related to fenofibrate therapy appear to be dose related. Hepatocellular, chronic active and cholestatic hepatitis associated with fenofibrate therapy have been reported after exposures of weeks to several years. In extremely rare cases, cirrhosis has been reported in association with chronic active hepatitis.
Regular periodic monitoring of liver function, including serum ALT (SGPT) should be performed for the duration of therapy with Fenofibrate, and therapy discontinued if enzyme levels persist above three times the normal limit.
Cholelithiasis :
Fenofibrate may increase cholesterol excretion into the bile, leading to cholelithiasis. If cholelithiasis is suspected, gallbladder studies are indicated. **FENO-TG** 160 mg Tablets therapy should be discontinued if gallstones are found.
Concomitant Oral Anticoagulants :
Caution should be exercised when anticoagulants are given in conjunction with **FENO-TG** 160 mg Tablets because of the potentiation of coumarin-type anticoagulants in prolonging the prothrombin time/INR. The dosage of the anticoagulant should be reduced to maintain the prothrombin time/INR at the desired level to prevent bleeding complications. Frequent prothrombin time/INR determinations are advisable until it has been definitely determined that the prothrombin time/INR has stabilized.
Concomitant HMG-CoA Reductase Inhibitors
The combined use of **FENO-TG** 160 mg Tablets and HMG-CoA reductase inhibitors should be avoided unless the benefit of further alterations in lipid levels is likely to outweigh the increased risk of this drug combination.
The combined use of fibric acid derivatives and HMG-CoA reductase inhibitors has been associated, in the absence of a marked pharmacokinetic interaction, with rhabdomyolysis, markedly elevated creatine kinase (CK) levels and myoglobinuria, leading in a high proportion of cases to acute renal failure.
The use of fibrates alone may occasionally be associated with myositis, myopathy, or rhabdomyolysis. Patients receiving **FENO-TG** 160 mg

D.I.FNC.MAL.E-03

Tablets and complaining of muscle pain, tenderness, or weakness should have prompt medical evaluation for myopathy, including serum creatine kinase level determination. If myopathy/myositis is suspected or diagnosed, **FENO-TG** 160 mg Tablets therapy should be stopped.
Mortality : The effect of fenofibrate on coronary heart disease morbidity and mortality and non-cardiovascular mortality has not been established.

PRECAUTIONS :
Initial therapy :
Laboratory studies should be done to ascertain that the lipid levels are consistently abnormal before instituting fenofibrate therapy. Every attempt should be made to control serum lipids with appropriate diet, exercise, weight loss in obese patients, and control of any medical problems such as diabetes mellitus and hypothyroidism that are contributing to the lipid abnormalities. Medications known to exacerbate hypertriglyceridemia (beta-blockers, thiazides, estrogens) should be discontinued or changed if possible prior to consideration of triglyceride-lowering drug therapy.
Continued therapy :
Periodic determination of serum lipids should be obtained during initial therapy in order to establish the lowest effective dose of fenofibrate. Therapy should be withdrawn in patients who do not have an adequate response after two months of treatment with the maximum recommended dose.
Pancreatitis :
Pancreatitis has been reported in patients taking fenofibrate, gemfibrozil, and clofibrate. This occurrence may represent a failure of efficacy in patients with severe hypertriglyceridemia, a direct drug effect, or a secondary phenomenon mediated through biliary tract stone or sludge formation with obstruction of the common bile duct.
Hypersensitivity Reactions :
Acute hypersensitivity reactions including severe skin rashes requiring patient hospitalization and treatment with steroids have occurred very rarely during treatment with fenofibrate, including rare spontaneous reports of Stevens-Johnson syndrome, and toxic epidermal necrolysis. Urticaria was seen in 1.1, and rash in 1.4 of fenofibrate patients.
Hematologic Changes :
Mild to moderate hemoglobin, hematocrit, and white blood cell decreases have been observed in patients following initiation of fenofibrate therapy. However, these levels stabilize during long-term administration. Extremely rare spontaneous reports of thrombocytopenia and agranulocytosis have been reported during post-marketing surveillance. Periodic blood counts are recommended during the first 12 months of fenofibrate administration.
Skeletal muscle :
The use of fibrates alone may occasionally be associated with myopathy. Treatment with drugs of the fibrate class has been associated on rare occasions with rhabdomyolysis, usually in patients with impaired renal function. Myopathy should be considered in any patient with diffuse myalgias, muscle tenderness or weakness, and/or marked elevations of creatine phosphokinase levels.
Patients should be advised to report promptly unexplained muscle pain, tenderness or weakness, particularly if accompanied by malaise or fever. CPK levels should be assessed in patients reporting these symptoms, and fenofibrate therapy should be discontinued if markedly elevated CPK levels occur or myopathy is diagnosed.
Pregnancy and& Nursing mothers :
Fenofibrate has not shown any teratogenic effects. However, there is no conclusion to the absence of congenital malformations in human. There is no information of the passage of fenofibrate into the mother's milk. Therefore, it is recommended not to use in pregnant & lactating women.
Pediatric Use :
Safety and efficacy in pediatric patients have not been established.
Geriatric Use :
Fenofibric acid is known to be substantially excreted by the kidney, and the risk of adverse reactions to this drug may be greater in patients with impaired renal function. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection.

DRUG INTERACTIONS :
Oral Anticoagulants :
CAUTION SHOULD BE EXERCISED WHEN COUMARIN ANTICOAGULANTS ARE GIVEN IN CONJUNCTION WITH FENO-TG 160 MG TABLETS. THE DOSAGE OF THE ANTICOAGULANTS SHOULD BE REDUCED TO MAINTAIN THE PROTHROMBIN TIME/INR AT THE DESIRED LEVEL TO PREVENT BLEEDING COMPLICATIONS. FREQUENT PROTHROMBIN TIME/INR DETERMINATIONS ARE ADVISABLE UNTIL IT HAS BEEN DEFINITELY DETERMINED THAT THE PROTHROMBIN TIME/INR HAS STABILIZED.
Concurrent use of lovastatin (or other HMG-CoA reductase inhibitors) may cause severe myositis and myoglobinuria.
Resins :
Since bile acid sequestrants may bind other drugs given concurrently, patients should take **FENO-TG** 160 mg Tablets at least 1 hour before or 4-6 hours after a bile acid binding resin to avoid impeding its absorption.
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 **FENO-TG** 160 mg Tablets, there is a risk that an interaction will lead to deterioration. The benefits and risks of using **FENO-TG** 160 mg Tablets with immunosuppressants and other potentially nephrotoxic agents should be carefully considered, and the lowest effective dose employed.

SIDE EFFECTS :
Adverse events reported by 2% or more of patients treated with fenofibrate are: BODY AS A WHOLE : Abdominal Pain, Back Pain, Headache, Asthenia, Flu Syndrome; DIGESTIVE : Liver Function Tests Abnormal, Diarrhea, Nausea, Constipation; METABOLIC AND NUTRITIONAL DISORDERS : SGPT Increased, Creatine Phosphokinase Increased, SGOT Increased; RESPIRATORY : Respiratory Disorder, Rhinitis. Increases in liver function tests were the most frequent events.
Additional adverse events reported are listed below.
MUSCULOSKELETAL SYSTEM : Myositis, myalgia, arthralgia, arthritis, tenosynovitis, joint disorder, arthrosis, leg cramps, bursitis, and myasthenia.

OVERDOSE :
There is no specific treatment for overdose with **FENO-TG** 160 mg Tablets. 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. Because fenofibrate is highly bound to plasma proteins, hemodialysis should not be considered.

STORAGE :
Store below 30°C, protected from light.

PRESENTATION :
FENO-TG 160 mg Tablets (Fenofibrate Tablets) is available in a blister of 10 tablets.

DATE OF REVISION :
16/06/2021

Product Registration Holder :
Unimed Sdn. Bhd.
No. 53. Jalan Tembaga SD 5/2B,
Bandar Sri Damansara,
52200 Kuala Lumpur, Malaysia

Manufactured by :
Troikaa
Troikaa Pharmaceuticals Ltd.
C-1, Sara Industrial Estate, Selaqui, Dehradun, Uttarakhand, India
D.I.FNC.MAL.E-03