Tigirate®

Fenofibrate

Description: Fenofibrate (**Tigirate®**) is a lipid regulating agent for oral administration, and acts through reductions of total cholesterol, LDL cholesterol, apolipoprotein B, total triglycerides and triglyceride rich lipoprotein (VLDL).

Mode of action: Fenofibric acid, the active metabolite of fenofibrate (**Tigirate®**), produces reduction in total cholesterol, LDL cholesterol, apolipoprotein B, total triglycerides and triglyceride rich lipoprotein (VLDL) in treated patients. In addition, treatment with fenofibrate results in increases in high-density lipoprotein (HDL) and apoproteins apoAI and apoAII.
Fenofibric acid activates Peroxisome Proliferator Activated Receptor type α (PPARα). 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 PPARα also induces an increase in the synthesis of apoproteins AI, AII and HDL-cholesterol. Fenofibrate also reduces serum uric acid levels in hyperuricemic and normal individuals by increasing the urinary excretion of uric acid.

Pharmacokinetics: *Absorption:* The unchanged compound is not recovered in the plasma. Fenofibric acid is the major plasma metabolite. Peak plasma concentration occurs after a mean period of 5 hours following dosing. Mean plasma concentration is 15 mcg/ml for a daily dose of 200 mg of fenofibrate. Steady state levels are observed throughout continuous treatments.
Distribution: Fenofibric acid is highly bound to plasma albumin; it can displace antivitamin K compounds from protein binding sites and may potentiate their anti-coagulant effect.
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.
Elimination: The product is mainly excreted in the urine; 70% in 24 hours and 88% in 6 days, at which time the total excretion in urine and faeces reaches 93%. Fenofibrate is mainly excreted as fenofibric acid and its derived glucuroconjugate. The plasma half-life of elimination of fenofibric acid is approximately 20 hours.

Composition: Tigirate® 200 mg Capsule: Each capsule contains fenofibrate BP 200 mg.

Indications: Fenofibrate (**Tigirate®**) is indicated as adjunctive therapy to diet to reduce elevated LDL-C, total-C, triglycerides and Apo B, and to increase HDL-C in adult patients with primary hypercholesterolemia or mixed dyslipidemia (Fredrickson Types IIa and IIb).

Dosage & administration: Patients should be placed on an appropriate lipid-lowering diet before receiving fenofibrate (**Tigirate®**), and should continue this diet during treatment. The recommended initial dose is one capsule taken daily during a main meal. In elderly patients without renal impairment, the normal adult dose is recommended. Since it is less well absorbed from an empty stomach, fenofibrate should always be taken with food. Response to therapy should be monitored by determination of serum lipid values. But treatment should be discontinued if an adequate response has not been achieved within three months.

Contraindications: Fenofibrate (**Tigirate®**) is contraindicated in children, in patients with severe liver dysfunction, gallbladder disease, biliary cirrhosis, severe renal disorders, and in patients hypersensitive to fenofibrate or any component of this medication, known photoallergy or phototoxic reaction during treatment with fibrates or ketoprofen.

Side effects: Adverse reactions observed during fenofibrate (**Tigirate®**) treatment are not very frequent (2 - 4 % of cases); they are generally minor & transient. The most commonly reported adverse reactions include; *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. sun lamp); *Neurological disorders:* Headache; *General disorders:* Fatigue; *Disorders of the ear:* Vertigo.

Use in pregnancy & lactation: Pregnancy Category C. There are no adequate data from the use of fenofibrate in pregnant women. Animal studies have not demonstrated any teratogenic effects. Embryotoxic effects have been shown at doses in the range of maternal toxicity. The potential risk for humans is unknown. There are no data on the excretion of fenofibrate and/or its metabolites into breast milk. It is therefore recommended that fenofibrate should not be administered to women who are pregnant or are breast-feeding.

Precautions: 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. Periodic determination of serum lipids should be obtained during initial therapy. Therapy should be withdrawn in patients who do not have an adequate response after two months of treatment with the maximum recommended dose of 200 mg per day. Periodic blood counts are recommended during the first 12 months of fenofibrate administration. 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 (Creatine Phospho Kinase) 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.

Drug Interactions: Caution should be exercised when caumarin anticoagulant are given in conjunction with fenofibrate. The combined use of fenofibrate 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. Since bile acid sequestrants may bind other drugs given concurrently, patients should take fenofibrate at least 1 hour before or 4 to 6 hours after a bile acid binding resin to avoid impeding its absorption. 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.

Over dosage: No case of over dosage with fenofibrate has been reported. No specific antidote is known. If overdose is suspected, treat symptomatically and institute appropriate supportive measures as required. Fenofibrate cannot be eliminated by haemodialysis.

Storage: Store in a cool and dry place, protected from light.

Packaging
Tigirate® 200 mg Capsule: Each carton contains 10X3 capsules in blister pack.

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Opsonin Pharma
Ideas for healthcare

Manufactured by
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