Fenofibrate

Category:

Antihyperlipidemic agent

Mechanism of action:

Fenofibric acid, the active metabolite of Fenofibrate, produces reductions 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.

Fenofibrate also reduces serum uric acid levels in hyperuricemic and normal individuals by increasing the urinary excretion of uric acid.

Pharmacokinetics:

Absorption: Fenofibrate is well absorbed from the GI tract. Peak plasma levels of fibric acid occur within 3 to 8 hours (depending on product) after administration, and steady state plasma levels are achieved within 5 to 7 days of dosing.

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.

Excretion: After absorption, Fenofibrate is mainly excreted in the urine in the form of metabolites, primarily fenofibric acid and fenofibric acid glucuronide.

Fenofibrate is eliminated with a half-life of 16-23 hours.

Indications:

- Treatment of Hypercholesterolemia
- Treatment of Hypertriglyceridemia
- Combination therapy with statins for mixed dyslipidemia

Administration and Dosage:

Maximum dose: 200 mg/day; varies by indication and product.

Hypertriglyceridemia: 200mg/day

Mixed hyperlipidemia, initial dose: 200 mg/day

Primary hypercholesterolemia, initial dosage: 200 mg/day

Children: safety and efficacy in children have not been established.

Contraindications:

Hepatic dysfunction, including primary biliary cirrhosis, and unexplained, persistent liver abnormality; several renal dysfunction; preexisting gallbladder disease; hypersensitivity to fenofibrate

Precautions:

- Cholelithiasis: fenofibrate, like clofibrate and gembibrozil, may increase cholesterol excretion into the bile, leading to cholelithiasis.
- Hepatic effects: fenofibrate is associated with increases in serum transaminase (AST or ALT).
- Hematologic changes: mild to moderate hemoglobin, hematocrit, and white blood cell decreases have been observed in patients following initiation of fenofibrate therapy.
- Pancreatitis: pancreatitis has been reported in patients taking fenofibrate, gemfibrozil, and clofibrate.
- Skeletal muscle effects: the use of fibrate alone, including fenofibrate, may occasionally associated with myopathy. CPK levels in patients reporting muscle pain, tenderness, or weakness should be assessed, and discontinue therapy if markedly elevated CPK levels occur or myopathy is diagnosed.

Pregnancy and breast feeding:

Pregnancy: Category C

Lactation: Do not use fenofibrate in breast-feeding mothers.

Drug Interactions:

Fenofibrate and fenofibric acid are mild to moderate inhibitors of CYP2C9 and weak inhibitors of CYP2A6 and CYP2C19**.**

- Bile acid sequestrants (i.e., cholestyramine, colestipol): because bile acid sequestrants may bind other drugs given concurrently, advise patients to take fenofibrate at least 1 hour before or 4–6 hours after the resin.

- Anticoagulants, oral (e.g., warfarin): potentiation of coumarin-type anticoagulants has been observed with prolongation of the PT/INR. Frequent PT/INR determinations and anticoagulant dosage reduction are advisable.

- Cyclosporine: coadministration may lead to increase risk of nephrotoxicity. Carefully consider the benefits and risks of using fenofibrate with immunosuppressants and other potentially nephrotoxic agents, and employ the lowest effective dose.

- HMG-CoA reductase inhibitor: the combined use of fenofibrate and HMG-CoA reductase inhibitors has been associated with rhabdomyolysis, markedly elevated creatine kinase levels, and myoglobinuria, leading in a high proportion of cases to acute renal failure.

Side effects:

Common Adverse Effects

Abnormal liver function tests (e.g., increased ALT, AST), respiratory disorder, abdominal pain, back pain, headache, increased CK concentrations, diarrhea, nausea, rhinitis, constipation, asthenia, flu syndrome.

Storage:

- Store between 15-30 °C
- Protect from moisture and light
- Keep out of the reach of children

Packaging:

Fenofibrate is available as 200 mg capsules in a box of 30 tablets.