Finofib® Benta
Fenofibrate

FORMS AND PRESENTATION

Finofib® Benta: Film coated tablets: Box of 30.

COMPOSITION

Finofib® Benta: Each film coated tablet contains Fenofibrate 160mg.

Excipients: lactose, starch, croscarmellose sodium, crospovidone, povidone sodium lauryl sulphate, magnesium stearate, talc, polyvinyl alcohol, titanium dioxide, lecithin, xanthan gum.

PHARMACOLOGICAL PROPERTIES

Pharmacodynamic properties

Therapeutic class: Lipid modifying agents.

ATC code: C10AB05.

Fenofibrate is a fibric acid derivative whose lipid modifying effects reported in humans are mediated via activation of Peroxisome Proliferator Activated Receptor type alpha (PPARα).

Through activation of PPARα, 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 PPARα also induces an increase in the synthesis of apoproteins AI and AII.

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 AI and AII.

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.

Pharmacokinetic properties

Absorption

Maximum plasma concentrations (C_{max}) 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%). The plasma elimination half-life of fenofibric acid is approximately 20 hours.

Biotransformation

No unchanged Fenofibrate can be detected in the plasma where the principal metabolite is fenofibric acid.

Elimination

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 hemodialysis.

INDICATIONS

Finofib® Benta is indicated as an adjunct to diet and other non-pharmacological treatment (e.g. exercise, weight reduction) for the following:

- Treatment of severe hypertriglyceridemia with or without low HDL cholesterol.
- Mixed hyperlipidemia when a statin is contraindicated or not tolerated.
- Mixed hyperlipidemia in patients at high cardiovascular risk in addition to a statin when triglycerides and HDL cholesterol are not adequately controlled.

CONTRAINDICATIONS

- Hepatic insufficiency (including biliary cirrhosis and unexplained persistent liver function abnormality e.g. persistent elevations in serum transaminases).
- Renal insufficiency.
- Children (age below 18 years).
- Hypersensitivity to the active substance or to any of the excipients.
- Known photoallergy or phototoxic reaction during treatment with fibrates or ketoprofen.
- Gallbladder disease.
- Chronic or acute pancreatitis with the exception of acute pancreatitis due to severe hypertriglyceridemia.
- This medicine should not be taken in patients allergic to peanut or arachis oil or soya lecithin or related products due to the risk of hypersensitivity reactions.

PRECAUTIONS

- Liver function: As with other lipid 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 are monitored every 3 months during the first 12 months of treatment and thereafter periodically. Attention should be paid to patients who develop increase in transaminase levels and therapy should be discontinued if ASAT (SGOT) and ALAT (SGPT) levels increase to more than 3 times the upper limit of the normal range. When symptoms indicative of hepatitis occur (e.g. jaundice, pruritus), laboratory tests are to be conducted for verification and discontinuation of Fenofibrate therapy may be considered.
- Pancreas: Pancreatitis has been reported in patients taking Fenofibrate. 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, resulting in the obstruction of the common bile duct.
- 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 hypoalbuminemia 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.

Patients with pre-disposing factors for myopathy and/or rhabdomyolysis, including age above 70 years old, personal or familial history of hereditary muscular disorders, renal impairment, hypothyroidism and high alcohol intake, may be at an increased risk of developing rhabdomyolysis. For these patients, the putative benefits and risks of Fenofibrate therapy should be carefully weighed up.

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 reserved to patients with severe combined dyslipidemia 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 hyperlipidemic patients taking estrogens or contraceptives containing estrogens it should be ascertained whether the hyperlipidemia is of primary or secondary nature (possible elevation of lipid values caused by oral estrogen).
- This medicinal product contains lactose. Therefore patients with rare hereditary problems of galactose intolerance, Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.
- Renal function: Treatment should be interrupted in case of an increase in creatinine levels > 50% ULN (upper limit of normal).

It is recommended that creatinine is measured during the first 3 months after initiation of treatment and thereafter periodically.

Ability to drive and use machines

Fenofibrate has no influence on the ability to drive and use machines.

PREGNANCY AND LACTATION

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. Therefore, Fenofibrate should only be used during pregnancy after a careful benefit/risk assessment.

There are no data on the excretion of Fenofibrate and/or its metabolites into breast milk.

Consequently Fenofibrate should not be used in nursing mother.

DRUG INTERACTIONS

- 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. Therefore, this combination is not recommended.
- 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: The risk of serious muscle toxicity is increased if Fenofibrate is used concomitantly with HMG-CoA reductase inhibitors or other fibrates. Such combination therapy should be used with caution and patients monitored closely for signs of muscle toxicity.
- Cytochrome P450 enzymes: In vitro studies using human liver microsomes indicate that Fenofibrate and fenofibric acid are not inhibitors of cytochrome (CYP) P450 isoforms CYP3A4, CYP2D6, CYP2E1, or CYP1A2. They are weak inhibitors of CYP2C19 and CYP2A6, and mild-to-moderate inhibitors of CYP2C9 at therapeutic concentrations.

Patients co-administered Fenofibrate and CYP2C19, CYP2A6, and especially CYP2C9 metabolized drugs with a narrow therapeutic index should be carefully monitored and, if necessary, dose adjustment of these drugs is recommended.

ADVERSE EFFECTS

The most commonly reported adverse effects during Fenofibrate therapy are digestive, gastric or intestinal disorders.

The frequency of adverse reactions listed below is defined using the following convention: Common (≥ 1/100 to < 1/10); uncommon (≥ 1/1,000 to < 1/100); rare (≥ 1/10,000 to < 1/1,000); very rare (< 1/10,000; including isolated reports); not known (cannot be estimated from the available data).

- Blood and lymphatic system disorders: Decreased hemoglobin, decreased white blood cell count (rare).
- Immune system disorders: Hypersensitivity (rare).
- Nervous system disorders: Headache (uncommon).
- Vascular disorders: Thromboembolism (pulmonary embolism, deep vein thrombosis) (uncommon).
- Respiratory, thoracic and mediastinal disorders: Interstitial pneumopathies (not known).
- Gastrointestinal disorders: Gastrointestinal signs and symptoms (abdominal pain, nausea, vomiting, diarrhea, flatulence) moderate in severity (common); pancreatitis (uncommon).
- Hepatobiliary disorders: Increased transaminases (common); cholelithiasis (uncommon); hepatitis (rare).
- Skin and subcutaneous tissue disorders: Cutaneous hypersensitivity (e.g. Rashes, pruritus, urticaria) (uncommon); alopecia, photosensitivity reactions (rare).
- Musculoskeletal, connective tissue and bone disorders: Muscle disorder (e.g. myalgia, myositis, muscular spasms and weakness) (uncommon); rhabdomyolysis (not known).
- Reproductive system and breast disorders: Sexual dysfunction (uncommon).
- Investigations: Increased blood creatinine (uncommon); increased blood urea (rare).

DOSAGE AND ADMINISTRATION

Adults

The recommended dose is one Finofib® Benta tablet containing 160 mg Fenofibrate taken once daily.

Elderly patients

The usual adult dose is recommended.

Patients with renal impairment

Dosage reduction is required in patients with renal impairment. The use of dosage forms containing a lower dose of active ingredient is recommended in these patients.

Children

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

Hepatic disease

Patients with hepatic disease have not been studied.

Dietary measures initiated before therapy should be continued.

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

Method of administration

Finofib® Benta tablet should be swallowed whole during a meal.

OVERDOSAGE

Only anecdotal cases of Fenofibrate overdosage have been received. In the majority of cases no overdose symptoms were 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 hemodialysis.

STORAGE CONDITIONS

Store below 30°C.

Keep in original pack in intact conditions.

Date of revision: March 2014.

This is a medicament

- A medicament is a product which affects your health, and its consumption contrary to instructions is dangerous for you
- Follow strictly the doctor's prescription, the method of use, and the instructions of the pharmacist who sold the medicament
- The doctor and the pharmacist are experts in medicine, its benefits and risks
- Do not by yourself interrupt the period of treatment prescribed for you
- Do not repeat the same prescription without consulting your doctor
- Medicament: keep out of reach of children

Council of Arab Health Ministers
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