FENOFIBRIC ACID- fenofibric acid capsule, delayed release

A-S Medication Solutions

GENERAL INFORMATION

These highlights do not include all the information needed to use FENOFIBRIC ACID DELAYED-RELEASE CAPSULES safely and effectively. See full prescribing information for FENOFIBRIC ACID DELAYED-RELEASE CAPSULES.

FENOFIBRIC ACID delayed-release capsules for oral use

INITIAL U.S. APPROVAL: 2008

Recent Major Changes

Warnings and Precautions

Hypersensitivity Reactions (5.9)

INDICATIONS AND USAGE

Fenofibric acid delayed-release capsule is a peroxisome proliferator-activated receptor (PPAR) alpha agonist indicated as adjunctive therapy to diet to:

- Reduce TG in patients with severe hypertriglyceridemia (1.3).
- Reduce elevated LDL-C, Total-C, TG and Apo B, and to increase HDL-C in patients with primary hypercholesterolemia or mixed dyslipidemia (1.2).

Limitations of Use: Fenofibrate at a dose equivalent to 135 mg of fenofibric acid delayed-release capsule did not reduce coronary heart disease morbidity and mortality in patients with type 2 diabetes mellitus (5.1).

DOSAGE AND ADMINISTRATION

Initial U.S. Approval: 2008

Oral Delayed-Release Capsules: 45 mg and 135 mg (1.2).

Active liver disease (4.5.3).

Gallbladder disease (4.5.5).

Nursing mothers (4.8.3).

Known hypersensitivity to fenofibric acid or fenofibrate (4.5).

ADVERSE REACTIONS

See 17 for PATIENT COUNSELING INFORMATION and Medication Guide.

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1 INDICATIONS AND USAGE

1.1 Treatment of Severe Hypertriglyceridemia
Fenofibric acid delayed-release capsules are indicated as adjunctive therapy to diet to reduce triglycerides (TG) in patients with severe hypertriglyceridemia. Improving glycemic control in diabetic patients showing fasting chylomicronemia will usually obviate the need for pharmacological intervention. Markedly elevated levels of serum triglycerides (e.g., >2500 mg/dL) may increase the risk of developing pancreatitis. The effect of fenofibric acid delayed-release capsules therapy on reducing this risk has not been adequately studied.

1.2 Treatment of Primary Hypercholesterolemia or Mixed Dyslipidemia
Fenofibric acid delayed-release capsules are indicated as adjunctive therapy to diet to reduce elevated low-density lipoprotein cholesterol (LDL-C), total cholesterol (Total-C), triglycerides (TG), and apolipoprotein B (Apo B), and to increase high-density lipoprotein cholesterol (HDL-C) in patients with primary hypercholesterolemia or mixed dyslipidemia.

1.3 Limitations of Use
Fenofibrate at a dose equivalent to 135 mg of fenofibric acid delayed-release capsules did not reduce coronary heart disease morbidity and mortality in 2 large, randomized controlled trials of patients with type 2 diabetes mellitus [see WARNING AND PRECAUTIONS (5.1)].

1.4 General Considerations for Treatment
Laboratory studies should be performed to establish that lipid levels are abnormal before instituting fenofibric acid delayed-release capsules therapy. Every reasonable attempt should be made to control serum lipids with non-drug methods including appropriate diet, exercise, weight loss in obese patients, and control of any medical problems such as diabetes mellitus and hypothyroidism that may be contributing to the lipid abnormalities. Medications known to exacerbate hypertriglyceridemia (beta-blockers, thiazides, estrogen) should be discontinued or changed if possible, and excessive alcohol intake should be addressed before triglyceride-lowering drug therapy is considered. If the decision is made to use lipid-altering drugs, the patient should be instructed that this does not reduce the importance of adhering to diet.

Drug therapy is not indicated for patients who have elevations of chylomicrons and plasma triglycerides, but who have normal levels of VLDL.

2 DOSAGE AND ADMINISTRATION

2.1 General Considerations
Patients should be placed on an appropriate lipid-lowering diet before receiving fenofibric acid delayed-release capsules, and should continue this diet during treatment. Fenofibric acid delayed-release capsules can be taken without regard to meals. Patients should be advised to swallow fenofibric acid delayed-release capsules whole. Do not open, crush, dissolve, or chew capsules. Serum lipids should be monitored periodically.

2.2 Severe Hypertriglyceridemia
The initial dose of fenofibric acid delayed-release capsules is 45 to 135 mg once daily. Dosage should be individualized according to patient response, and should be adjusted if necessary following repeat lipid determinations at 4 to 8 week intervals. The maximum dose is 135 mg once daily.

2.3 Primary Hypercholesterolemia or Mixed Dyslipidemia
The dose of fenofibric acid delayed-release capsules is 135 mg once daily.

2.4 Impaired Renal Function
Treatment with fenofibric acid delayed-release capsules should be initiated at a dose of 45 mg once daily in patients with mild to moderate renal impairment and should only be increased after evaluation of the effects on renal function and lipid levels at this dose. The use of fenofibric acid delayed-release capsules should be avoided in patients with severely impaired renal function [see USE IN SPECIFIC POPULATIONS (8.6) and CLINICAL PHARMACOLOGY (12.3)].

2.5 Geriatric Patients
Dose selection for the elderly should be made on the basis of renal function [see USE IN SPECIFIC POPULATIONS (8.5)].

3 DOSAGE FORMS AND STRENGTHS

- Fenofibric acid delayed-release capsules, 45 mg have size “3” capsule with brown cap and yellow body, imprinted with “LU” on cap and “Q41” on body in black ink, containing four white to off white mini-tablets.
- Fenofibric acid delayed-release capsules, 135 mg have size “0” capsule with blue opaque cap and yellow opaque body, imprinted with “LU” on cap and “Q42” on body in black ink, containing twelve white to off white mini-tablets.

4 CONTRAINDICATIONS
Fenofibric acid is contraindicated in:
- patients with severe renal impairment, including those receiving dialysis [see CLINICAL PHARMACOLOGY (12.3)].
- patients with active liver disease, including those with primary biliary cirrhosis and unexplained persistent liver function abnormalities [see WARNINGS AND PRECAUTIONS (5.3)].
- patients with preexisting gallbladder disease [see WARNINGS AND PRECAUTIONS (5.5)].
- nursing mothers [see USE IN SPECIFIC POPULATIONS (8.3)].
- patients with hypersensitivity to fenofibric acid or fenofibrate [see WARNINGS AND PRECAUTIONS (5.9)].

5 WARNINGS AND PRECAUTIONS

5.1 Mortality and Coronary Heart Disease Morbidity
The effect of fenofibrate on coronary heart disease morbidity and mortality and non-cardiovascular mortality has not been established. Because of similarities between fenofibrate and fenofibrate, clofibrate, and gemfibrozil, the findings in the following large randomized, placebo-controlled clinical studies with these fibrates drugs may also apply to fenofibrate.

The Action to Control Cardiovascular Risk in Diabetes Lipid (ACCORD Lipid) trial was a randomized placebo-controlled study of 5558 patients with type 2 diabetes mellitus on background statin therapy treated with fenofibrate. The mean duration of follow-up was 4.7 years. Fenofibrate plus statin combination therapy showed a non-significant 8% relative risk reduction in the primary outcome of major adverse cardiovascular events (MACE), a composite of non-fatal myocardial infarction, non-fatal stroke, and cardiovascular death (hazard ratio [HR] 0.92 [95% CI 0.79 to 1.08] p = 0.32) as compared to statin monotherapy. In a gender subgroup analysis, the hazard ratio for MACE in men receiving combination therapy versus statin monotherapy was 0.82 (95% CI 0.69 to 0.99), and the hazard ratio for MACE in women receiving combination therapy versus statin monotherapy was 1.38 (95% CI 0.98 to 1.94) (interaction p = 0.01). The clinical significance of this subgroup finding is unclear.

The Fenofibrate Intervention and Event Lowering in Diabetes (FIELD) study was a 5-year randomized, placebo-controlled study of 9795 patients with type 2 diabetes mellitus treated with fenofibrate. Fenofibrate demonstrated a non-significant 11% relative risk reduction in the primary outcome of coronary heart disease events (hazard ratio [HR] 0.89, 95% CI 0.75 to 1.05, p = 0.10) and a significant 11% reduction in the secondary outcome of total cardiovascular disease events (HR 0.89 [0.80 to 0.99], p = 0.04). There was a non-significant 11% (HR 1.11 [0.95, 1.29], p = 0.10) and 19% (HR 1.19 [0.98, 1.51], p = 0.22) increase in total and coronary heart disease mortality, respectively, with fenofibrate as compared to placebo.

In the Coronary Drug Project, a large study of post-myocardial infarction patients treated for 5 years with clofibrate, there was no difference in mortality seen between the clofibrate group and the placebo group. There was, however, a difference in the rate of cholelithiasis and cholecystitis requiring surgery between the two groups (3.9% vs. 1.8%).

In a study conducted by the World Health Organization (WHO), 5000 subjects without known coronary artery disease were treated with placebo or clofibrate for 5 years and followed for an additional one year. There was a statistically significant, higher age-adjusted all-cause mortality in the clofibrate group compared with the placebo group (5.70% vs. 3.96%, p < 0.01). Excess mortality was due to a 33% increase in non-cardiovascular causes, including malignancy, post-cholecystectomy complications, and pancreatitis. This appeared to confirm the higher risk of gallbladder disease seen in clofibrate-treated patients studied in the Coronary Drug Project.

The Helsinki Heart Study was a large (N = 4081) study of middle-aged men without a history of coronary artery disease. Subjects received either placebo or gemfibrozil for 5 years, with a 3.5 year open extension afterward. Total mortality was numerically higher in the gemfibrozil randomization group but did not achieve statistical significance (p = 0.19, 95% confidence interval for relative risk G/P = 0.91 to 1.64). Although cancer deaths trended higher in the gemfibrozil group (p = 0.13), cancers (excluding basal cell carcinoma) were diagnosed with equal frequency in both study groups. Due to the limited size of the study, the relative risk of death from cancer was not shown to be different than that seen in the 9 year follow-up data from WHO study (HR = 1.29). A secondary prevention component of the Helsinki Heart Study enrolled middle-aged men excluded from the primary prevention study because of known or suspected coronary heart disease. Subjects received gemfibrozil or placebo for 5 years. Although cardiac deaths trended higher in the gemfibrozil group, this was not statistically significant (hazard ratio 2.2, 95% confidence interval: 0.94 to 5.05).

Data from observational studies suggest that the risk for rhabdomyolysis is increased when fibrates are co-administered with a statin.

Cases of myopathy, including rhabdomyolysis, have been reported with fibrates co-administered with colchicine, and caution should be exercised when prescribing fenofibrate with colchicine (see DRUG INTERACTIONS).

5.2 Skeletal Muscle

Fibrates increase the risk of myositis or myopathy and have been associated with rhabdomyolysis. The risk for serious muscle toxicity appears to be increased in elderly patients and in patients with diabetes, renal failure, or hypothyroidism.

Myopathy should be considered in any patient with diffuse myalgias, muscle tenderness or weakness, and/or marked elevation of CPK levels. Patients should promptly report 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 should be discontinued if markedly elevated CPK levels occur or myopathy or myositis is suspected or diagnosed.

Data from observational studies suggest that the risk for rhabdomyolysis is increased when fibrates are co-administered with a statin.

5.3 Liver Function

Fenofibrate at a dose of 125 mg once daily has been associated with increases in serum transaminases (AST [SGOT] or ALT [SGPT]). In a pooled analysis of three 12-week, double-blind, controlled studies of fenofibrate acid, increases in ALT and AST to > 3 times the upper limit of normal were observed in 1.8% and 2.2%, respectively, of patients receiving fenofibrate acid without other lipid-altering drugs. Increases in ALT and/or AST were not accompanied by increases in bilirubin or clinically significant increases in alkaline phosphatase.

In a pooled analysis of 10 placebo-controlled trials of fenofibrate, increases to > 3 times the upper limit of normal in ALT occurred in 6.3% of patients taking fenofibrate versus 1.1% of patients treated with placebo. The incidence of increases in transaminases observed with fenofibrate therapy may be dose related. In an 8-week dose-ranging study of fenofibrate in hypertriglyceridemia, the incidence of ALT or AST elevations ≥ 3 times the upper limit of normal was 13% in patients receiving doses equivalent to 50 mg to 135 mg fenofibrate acid once daily and was 6% in those receiving doses equivalent to 45 mg fenofibrate acid once daily or less, or placebo. Hepatocellular, chronic active, and cholestatic hepatitis observed 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.

Baseline and regular monitoring of liver function, including serum ALT (SGPT) should be performed for the duration of therapy with fenofibrate acid, and therapy discontinued if enzyme levels persist above 3 times the upper limit of normal.

5.4 Serum Creatinine

Reversible elevations in serum creatinine have been reported in patients receiving fenofibrate acid as well as patients receiving fenofibrate. In the pooled analysis of three 12-week, double-blind, controlled studies of fenofibrate acid, increases in creatinine to > 2 mg/dL occurred in 0.8% of patients treated with fenofibrate acid without other lipid-altering drugs. Elevations in serum creatinine were generally stable over time with no evidence for continued increases in serum creatinine with long-term therapy and tended to return to baseline following discontinuation of treatment. The clinical significance of these observations is unknown. Monitoring renal function in patients with renal impairment taking fenofibrate acid is suggested. Renal monitoring should be considered for patients at risk for renal insufficiency, such as the elderly and those with diabetes.

5.5 Cholelithiasis
Fenofibric acid, like fenofibrate, clofibrate, and gemfibrozil, may increase cholesterolemic excretion into the bile, potentially leading to cholelithiasis. If cholelithiasis is suspected, gallbladder studies are indicated. Fenofibric acid therapy should be discontinued if gallstones are found.

5.6 Coumarin Anticoagulants

Caution should be exercised when fenofibric acid is given in conjunction with oral coumarin anticoagulants. Fenofibric acid may potentiate the anticoagulant effects of these agents resulting in prolongation of the prothrombin time International Normalized Ratio (PT/INR). Frequent monitoring of PT/INR and dose adjustment of the oral anticoagulant are recommended until the PT/INR has stabilized in order to prevent bleeding complications (see DRUG INTERACTIONS (7.4)).

5.7 Pancreatitis

Pancreatitis has been reported in patients taking drugs of the fibrate class, including fenofibric acid. 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.

5.8 Hematological Changes

Mild to moderate hemoglobin, hematocrit, and white blood cell decreases have been observed in patients following initiation of fenofibric acid and fenofibrate therapy. However, these levels stabilize during long-term administration. Thrombocytopenia and agranulocytosis have been reported in individuals treated with fenofibrates. Periodic monitoring of red and white blood cell counts are recommended during the first 12 months of fenofibric acid administration.

5.9 Hypersensitivity Reactions

Acute Hypersensitivity

Urticaria was seen in 1.1% vs. 0%, and rash in 1.4% vs. 0.8% of fenofibrate and placebo patients respectively in controlled trials.

Delayed Hypersensitivity

Severe cutaneous adverse drug reactions (SCAR), including Stevens-Johnson syndrome, toxic epidermal necrolysis, and Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS), have been reported postmarketing, occurring days to weeks after initiation of fenofibrate. The cases of DRESS were associated with cutaneous reactions (such as rash or exfoliative dermatitis) and a combination of eosinophilia, fever, systemic organ involvement (renal, hepatic, or respiratory). Discontinue fenofibrate and treat patients appropriately if SCAR is suspected.

5.10 Venothromboembolic Disease

In the FIELD trial, pulmonary embolus (PE) and deep vein thrombosis (DVT) were observed at higher rates in the fenofibrate- than the placebo-treated group. Of 9,795 patients enrolled in FIELD, there were 4,900 in the placebo group and 4,895 in the fenofibrate group. For DVT, there were 48 events (1%) in the placebo group and 53 (1%) in the fenofibrate group (p = 0.022).

5.11 Paradoxical Decreases in HDL Cholesterol Levels

There have been postmarketing and clinical trial reports of severe decreases in HDL cholesterol levels (as low as 2 mg/dL) occurring in diabetic and non-diabetic patients initiated on fibrate therapy. The decrease in HDL-C is mirrored by a decrease in apolipoprotein A1. This decrease has been reported to occur within 2 weeks to months after initiation of fibrate therapy. It is recommended that HDL-C levels be checked within the first few months after initiation of fibrate therapy. If a severely depressed HDL-C level is detected, fibrate therapy should be withdrawn, and the HDL-C level monitored until it has returned to baseline, and fibrate therapy should not be re-initiated.

5.12 Other Adverse Reactions

5.12.1 Clinical Trials Experience

Because clinical studies are conducted under widely varying conditions, adverse reaction rates observed in the clinical studies of a drug cannot be directly compared to rates in the clinical studies of another drug and may not reflect the rates observed in practice.

Fenofibric acid is the active metabolite of fenofibrate. Adverse events reported by 2% or more of patients treated with fenofibrate and greater than placebo during double-blind, placebo-controlled trials are listed in Table 1. Adverse events leading to discontinuation of treatment in 5.0% of patients treated with fenofibrate and in 3.0% treated with placebo. Increases in liver tests were the most frequent events, leading to discontinuation of treatment in 5.0% of patients treated with fenofibrate.

<table>
<thead>
<tr>
<th>Event</th>
<th>Fenofibrate (N = 439)</th>
<th>Placebo (N = 365)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdominal Pain</td>
<td>4.6%</td>
<td>4.4%</td>
</tr>
<tr>
<td>Back Pain</td>
<td>3.4%</td>
<td>2.5%</td>
</tr>
<tr>
<td>Headache</td>
<td>3.2%</td>
<td>2.7%</td>
</tr>
<tr>
<td>Nausea</td>
<td>2.3%</td>
<td>1.9%</td>
</tr>
<tr>
<td>Constipation</td>
<td>2.1%</td>
<td>1.4%</td>
</tr>
<tr>
<td>Increased Creatine Phosphokinase</td>
<td>7.5%</td>
<td>1.4%</td>
</tr>
<tr>
<td>Increased AST</td>
<td>3.4%</td>
<td>0.5%</td>
</tr>
<tr>
<td>Increased ALT</td>
<td>3.0%</td>
<td>1.6%</td>
</tr>
<tr>
<td>Increased ALT</td>
<td>3.0%</td>
<td>1.4%</td>
</tr>
<tr>
<td>Respiratory Disorder</td>
<td>6.2%</td>
<td>5.5%</td>
</tr>
<tr>
<td>Rhinitis</td>
<td>2.3%</td>
<td>1.1%</td>
</tr>
</tbody>
</table>

* Dosage equivalent to 135 mg fenofibric acid

Urticaria was seen in 1.1% vs. 0%, and rash in 1.4% vs. 0.8% of fenofibrate and placebo patients respectively in controlled trials.

Clinical trials with fenofibric acid did not include a placebo-control arm. However, the adverse event profile of fenofibric acid was generally consistent with that of fenofibrate. The following adverse events not listed above were reported in 2.3% of patients taking fenofibric acid alone:
CONTRAINDICATIONS
The use of fenofibric acid has not been evaluated in subjects with hepatic impairment.

Hepatic Impairment
Monitoring renal function in patients with renal impairment is recommended.

Renal Impairment
Elderly patients with normal renal function should require no dose modifications. Consider monitoring
creatinine clearance and rises in serum creatinine, and because renal excretion is the primary elimination
route of drugs of the fibrate class including fenofibric acid, there is a risk that an interaction will lead
to deterioration of renal function. The benefits and risks of using fenofibric acid with
immunosuppressants and other potentially nephrotoxic agents should be carefully considered, and the
lowest effective dose employed.

Geriatric Use
Fenofibric acid is substantially excreted by the kidney as fenofibric acid and fenofibric acid
glucuronide, and the risk of adverse reactions to this drug may be greater in patients with impaired renal
function. Fenofibric acid exposure is not influenced by age. Since elderly patients have a higher
incidence of renal impairment, dose selection for the elderly should be made on the basis of renal
function [see DOSAGE AND ADMINISTRATION (2.5) and CLINICAL PHARMACOLOGY (12.3)].
Elderly patients with normal renal function should require no dose modifications. Consider monitoring
renal function in elderly patients taking fenofibric acid.

Pediatric Use
The use of fenofibric acid should be avoided in patients who have severe renal impairment [see
CONTRAINDICATIONS (8) and CLINICAL PHARMACOLOGY (12.3)].

8.7 Hepatic Impairment
The use of fenofibric acid has not been evaluated in subjects with hepatic impairment [see
CONTRAINDICATIONS (8) and CLINICAL PHARMACOLOGY (12.3)].
10 OVERDOSAGE
There is no specific treatment for overdose with fenofibric acid. 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 fenofibric acid is highly bound to plasma proteins, hemodialysis should not be considered.

11 DESCRIPTION
Fenofibric acid is a lipid regulating agent available as delayed release capsules for oral administration. Each delayed-release capsule contains choline fenofibrate, equivalent to 45 mg or 135 mg of fenofibric acid. The chemical name for choline fenofibrate is ethanaminium, 2-hydroxy-N,N,N-trimethyl, 2-(4-(4-chlorobenzoyl)phenoxy)-2-methylpropanoate (1:1) with the following structural formula:

![Choline Fenofibrate](image)

The empirical formula is C_{22}H_{24}ClNO_{5}, and the molecular weight is 421.91. Choline fenofibrate is freely soluble in water. The melting point is approximately 210°C. Choline fenofibrate is a white to yellow powder, which is stable under ordinary conditions.

Each delayed-release capsule contains enteric coated mini-tablets comprised of choline fenofibrate and the following inactive ingredients: colloidal silicon dioxide, dibutyl sebacate, ethyl cellulose, hypromellose, lactose monohydrate, magnesium stearate, metacrylic acid copolymer, povidone, sodium starchyl fumarate, talc and triethyl citrate. The capsule shell of the 45 mg capsule contains the following inactive ingredients: FD and C Blue #1, gelatin, iron oxide yellow, sodium lauryl sulphate and titanium dioxide. The capsule shell of the 135 mg capsule contains the following inactive ingredients: FD and C Blue #1, gelatin, iron oxide black, potassium chloride, potassium ferricyanide, propylene glycol and shellac.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action
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 α (PPARα). Through this mechanism, fenofibric acid increases lipolysis and elimination of triglyceride-rich particles from plasma by activating lipoprotein lipase and reducing production of Apo CIII (an inhibitor of lipoprotein lipase activity). The activation of PPARα also induces an increase in the synthesis of HDL-C and Apo AI and AII.

12.3 Pharmacokinetics
Fenofibric acid delayed-release capsules contain fenofibric acid, which is the only circulating pharmacologically active moiety in plasma after oral administration of fenofibric acid delayed-release capsules. Fenofibric acid is also the circulating pharmacologically active moiety in plasma after oral administration of fenofibrate, the ester of fenofibric acid.

Plasma concentrations of fenofibric acid after administration of one 135 mg fenofibric acid delayed-release capsule are equivalent to those after one 200 mg capsule of micronized fenofibrate administered under fed conditions.

Absorption
Fenofibric acid is well absorbed throughout the gastrointestinal tract. The absolute bioavailability of fenofibric acid is approximately 81%.

Peak plasma levels of fenofibric acid occur within 4 to 5 hours after a single dose administration of fenofibric acid delayed-release capsule under fasting condition. Fenofibric acid exposure in plasma, as measured by Cmax and AUC, is not significantly different when a single 135 mg dose of fenofibric acid delayed-release capsule is administered under fasting or nonfasting condition.

Distribution
Upon multiple dosing of fenofibric acid delayed-release capsules, fenofibric acid levels reach steady state within 8 days. Plasma concentrations of fenofibric acid at steady state are approximately slightly more than double those following a single dose. Serum protein binding is approximately 99% in normal and dyslipidemic subjects.

Metabolism
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.

In vivo metabolism data after fenofibrate administration indicate that fenofibric acid does not undergo oxidative metabolism (e.g., cytochrome P450) to a significant extent.

Elimination
After absorption, fenofibric acid is primarily excreted in the urine in the form of fenofibric acid and fenofibric acid glucuronide.

Fenofibric acid is eliminated with a half-life of approximately 20 hours, allowing once daily administration of fenofibric acid delayed-release capsules.

Specific Populations
Geriatrics:
In five 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 an equivalent dose of fenofibric acid delayed-release capsules can be used in elderly subjects with normal renal function, without increasing accumulation of the drug or metabolites [see USE IN SPECIFIC POPULATIONS (8.5)].

Pediatrics:
The pharmacokinetics of fenofibric acid has not been studied in pediatric populations.

Gender:
No pharmacokinetic difference between males and females has been observed for fenofibric acid delayed-release capsules.

Race:
The influence of race on the pharmacokinetics of fenofibric acid delayed-release capsules has not been studied; however, fenofibric acid is not metabolized by enzymes known for exhibiting inter-ethnic variability.

**Renal Impairment:**

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 [eGFR] <30 mL/min/1.73m²) showed a 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 to 59 mL/min/1.73m²) 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 fenofibric acid delayed-release capsules should be avoided in patients who have severe renal impairment and dose reduction is required in patients having mild to moderate renal impairment [see DOSAGE AND ADMINISTRATION (2.4)].

**Hepatic Impairment:**

No pharmacokinetic studies have been conducted in patients with hepatic impairment.

**Drug-drug Interactions**

In vitro studies using human liver microsomes indicate that fenofibric acid is not an inhibitor of cytochrome (CYP) 450 isoforms CYP3A4, CYP2D6, CYP2E1, or CYP1A2. It is a weak inhibitor of CYP2C9, CYP3A4, and CYP2C9, and mild-to-moderate inhibitor of CYP2C9 at therapeutic concentrations.

Comparison of atorvastatin exposures when atorvastatin (80 mg once daily for 10 days) is given in combination with fenofibric acid delayed-release capsules 135 mg once daily for 10 days) and ezetimibe (10 mg once daily for 10 days) versus when atorvastatin is given in combination with ezetimibe only (ezetimibe 10 mg once daily and atorvastatin, 80 mg once daily for 10 days): The C\text{max} increased by 1% for atorvastatin and ortho-hydroxy-atorvastatin, respectively, and did not change for para-hydroxy-atorvastatin.

Comparison of ezetimibe exposures when ezetimibe (10 mg once daily for 10 days) is given in combination with fenofibric acid (fenofibric acid delayed-release capsules 135 mg once daily for 10 days) and atorvastatin (80 mg once daily for 10 days) versus when ezetimibe is given in combination with atorvastatin only (ezetimibe 10 mg once daily and atorvastatin, 80 mg once daily for 10 days): The C\text{max} increased by 26% and 9% for total and free ezetimibe, respectively. The AUC increased by 27% and 12% for total and free ezetimibe, respectively.

Table 2 describes the effects of co-administered drugs on fenofibric acid systemic exposure. Table 3 describes the effects of co-administered fenofibrate on other drugs.

### Table 2. Effects of Co-Administered Drugs on Fenofibric Acid Systemic Exposure from Fenofibric Acid Delayed-Release Capsules or Fenofibrate Administration

<table>
<thead>
<tr>
<th>Co-Administered Drug</th>
<th>Dosage Regimen of Co-Administered Drug</th>
<th>Dosage Regimen of Fenofibric Acid Delayed-Release Capsules or Fenofibrate</th>
<th>Changes in Fenofibric Acid Exposure</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>AUC</td>
<td>(C_{\text{max}})</td>
</tr>
<tr>
<td>Lipid-lowering agents</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rosuvastatin</td>
<td>40 mg once daily for 10 days</td>
<td>Fenofibric acid delayed-release capsules 135 mg once daily for 10 days</td>
<td>12%</td>
</tr>
<tr>
<td>Atorvastatin</td>
<td>20 mg once daily for 10 days</td>
<td>Fenofibrate 160 mg* once daily for 10 days</td>
<td>14%</td>
</tr>
<tr>
<td>Ancevastatin</td>
<td>10 mg once daily for 10 days</td>
<td>Fenofibric acid delayed-release capsules 135 mg once daily for 10 days</td>
<td>75%</td>
</tr>
<tr>
<td>Pravastatin</td>
<td>40 mg as a single dose</td>
<td>Fenofibrate 3 x 67 mg* as a single dose</td>
<td>1%</td>
</tr>
<tr>
<td>Fluvastatin</td>
<td>40 mg as a single dose</td>
<td>Fenofibrate 160 mg* as a single dose</td>
<td>10%</td>
</tr>
<tr>
<td>Simvastatin</td>
<td>80 mg once daily for 7 days</td>
<td>Fenofibrate 160 mg* as a single dose</td>
<td>11%</td>
</tr>
<tr>
<td>Anti-diabetic agents</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Glimepiride</td>
<td>8 mg as a single dose</td>
<td>Fenofibrate 145 mg* once daily for 14 days</td>
<td>11%</td>
</tr>
<tr>
<td>Metformin</td>
<td>850 mg 3 times daily for 10 days</td>
<td>Fenofibrate 145 mg* once daily for 14 days</td>
<td>17%</td>
</tr>
<tr>
<td>Rosiglitazone</td>
<td>8 mg once daily for 5 days</td>
<td>Fenofibrate 145 mg* once daily for 14 days</td>
<td>11%</td>
</tr>
<tr>
<td>†</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Omeprazole</td>
<td>40 mg once daily for 5 days</td>
<td>Fenofibrate acid delayed-release capsules 135 mg as a single dose fasting</td>
<td>16%</td>
</tr>
<tr>
<td>‡</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Omeprazole</td>
<td>40 mg once daily for 5 days</td>
<td>Fenofibrate acid delayed-release capsules 135 mg as a single dose with food</td>
<td>19%</td>
</tr>
</tbody>
</table>

### Table 3. Effects of Fenofibrate Acid Delayed-Release Capsules or Fenofibrate Co-Administration on Systemic Exposure of Other Drugs

<table>
<thead>
<tr>
<th>Dosage Regimen of Fenofibrate Acid Delayed-Release Capsules or Fenofibrate</th>
<th>Change in Co-Administered Drug Exposure</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>AUC</td>
</tr>
<tr>
<td>Lipid-lowering agents</td>
<td></td>
</tr>
<tr>
<td>Fenofibrate acid delayed-release capsules 135 mg as a single dose</td>
<td></td>
</tr>
<tr>
<td>Rosuvastatin, 40 mg once daily for 10 days</td>
<td>16%</td>
</tr>
<tr>
<td>Fenofibrate 160 mg* once daily for 10 days</td>
<td>17%</td>
</tr>
<tr>
<td>Fenofibrate 3 x 67 mg* as a single dose</td>
<td>13%</td>
</tr>
<tr>
<td>Pravastatin, 40 mg as a single dose</td>
<td></td>
</tr>
<tr>
<td>Fluvastatin, 40 mg as a single dose</td>
<td>15%</td>
</tr>
<tr>
<td>Fenofibrate 145 mg* once daily for 14 days</td>
<td>12%</td>
</tr>
<tr>
<td>Anti-diabetic agents</td>
<td></td>
</tr>
<tr>
<td>Glimepiride, 8 mg as a single dose</td>
<td>13%</td>
</tr>
<tr>
<td>Metformin, 850 mg 3 times daily for 10 days</td>
<td>13%</td>
</tr>
<tr>
<td>Rosiglitazone, 8 mg once daily for 5 days</td>
<td>13%</td>
</tr>
</tbody>
</table>

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

**Fenofibric Acid**

No carcinogenicity and fertility studies have been conducted with choline fenofibrate or fenofibric acid. However, because fenofibrate is rapidly converted to its active metabolite, fenofibric acid, either during or immediately following absorption both in animals and humans, studies conducted with fenofibrate are relevant for the assessment of the toxicity profile of fenofibric acid. A similar toxicity spectrum is expected after treatment with either fenofibric acid delayed-release capsules or fenofibrate.

**Fenofibrate**

Two dietary carcinogenicity studies have been conducted in rats with fenofibrate. In the first 24-month study, Wistar rat were dosed with fenofibrate at 10, 45, and 200 mg/kg/day, approximately 0.3, 1, and 6 times the maximum recommended human dose (MRHD), based on body surface area comparisons (mg/m²). At a dose of 200 mg/kg/day (6 times the MRHD), the incidence of liver carcinomas was significantly increased in both sexes. A statistically significant increase in pancreatic carcinomas was observed in males at 1 and 6 times the MRHD; an increase in pancreatic adenomas and benign testicular interstitial cell tumors was observed at 6 times the MRHD in males. In a second 24-month rat carcinogenicity study in a different strain of rats (Sprague-Dawley), doses of 10 and 60 mg/kg/day (0.3 and 2 times the MRHD), produced significant increases in the incidence of pancreatic acinar adenomas in both sexes and increases in interstitial cell tumors of the testes at 2 times the MRHD.
A 117-week carcinogenicity study was conducted in rats comparing three drugs: fenofibrate 10 and 60 mg/kg/day (0.3 and 2 times the MRHD), clofibrate (400 mg/kg/day; 2 times the human dose), and gemfibrozil (250 mg/kg/day; 2 times the MRHD). Fenofibrate increased pancreatic acinar adenomas in both sexes. Clofibrate increased hepatic carcinomas and pancreatic acinar adenomas in males and hepatic neoplastic nodules in females. Gemfibrozil increased hepatic neoplastic nodules in males and females, while all three drugs increased testicular interstitial cell tumors in males.

In a 21-month study in CF-1 mice, fenofibrate 10, 45, and 200 mg/kg/day (approximately 0.2, 1, and 3 times the MRHD on the basis of mg/kg body surface area) significantly increased the liver carcinomas in both sexes at 3 times the MRHD. In a second 18-month study at 10, 60, and 200 mg/kg/day, fenofibrate significantly increased the liver carcinomas in male and female mice at 3 times the MRHD.

Electron microscopy studies have demonstrated peroxisome proliferation following fenofibrate administration to the rat. An adequate study to test for peroxisome proliferation in humans has not been done, but changes in peroxisome morphology and numbers have been noted in humans after treatment with other members of the fibrate class when liver biopsies were compared before and after treatment in the same individual.

**Mutagenesis**

Fenofibrate has been demonstrated to be devoid of mutagenic potential in the following tests: Ames, mouse lymphoma, chromosomal aberration and sister chromatid exchange in human lymphocytes, and unscheduled DNA synthesis in primary rat hepatocytes.

**Impairment of Fertility**

In a fertility study, rats were given oral dietary doses of fenofibrate. Males received doses for 61 days prior to mating and females for 15 days prior to mating through weaning, which resulted in no adverse effect on fertility at doses up to 360 mg/kg/day (~10 times the MRHD, based on mg/m² body surface area comparison).

### 14 CLINICAL STUDIES

#### 14.1 Severe Hypertriglyceridemia

The effects of fenofibrate on serum triglycerides were studied in two randomized, double-blind, placebo-controlled clinical trials of 147 hypertriglyceridemic patients. Patients were treated for eight weeks under protocols that differed only in that one entered patients with baseline TG levels of 500 to 1500 mg/dL, and the other TG levels of 350 to 500 mg/dL. In patients with hypertriglyceridemia and normal cholesterolemia with or without hypercholesterolemia, treatment with fenofibrate at dosages equivalent to 135 mg once daily of fenofibric acid delayed-release capsules decreased primarily VLDL-TG and VLDL-C. Treatment of patients with elevated TG often results in an increase of LDL-C (Table 4).

### Table 4. Effects of Fenofibrate in Patients With Severe Hypertriglyceridemia

<table>
<thead>
<tr>
<th>Study 1</th>
<th>Baseline TG levels 350 to 499 mg/dL</th>
<th>N</th>
<th>Baseline Mean (mg/dL)</th>
<th>Endpoint Mean (mg/dL)</th>
<th>Mean % Change</th>
<th>N</th>
<th>Baseline Mean (mg/dL)</th>
<th>Endpoint Mean (mg/dL)</th>
<th>Mean % Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>Triglycerides</td>
<td>28</td>
<td>449</td>
<td>450</td>
<td>-0.5</td>
<td>27</td>
<td>432</td>
<td>223</td>
<td>-46.2*</td>
<td></td>
</tr>
<tr>
<td>VLDL Triglycerides</td>
<td>19</td>
<td>367</td>
<td>350</td>
<td>2.7</td>
<td>19</td>
<td>350</td>
<td>178</td>
<td>-44.1*</td>
<td></td>
</tr>
<tr>
<td>HDL Cholesterol</td>
<td>28</td>
<td>255</td>
<td>261</td>
<td>2.8</td>
<td>27</td>
<td>252</td>
<td>227</td>
<td>-9.1*</td>
<td></td>
</tr>
<tr>
<td>LDL Cholesterol</td>
<td>28</td>
<td>120</td>
<td>129</td>
<td>12</td>
<td>27</td>
<td>128</td>
<td>137</td>
<td>14.5</td>
<td></td>
</tr>
<tr>
<td>VLDL Cholesterol</td>
<td>27</td>
<td>99</td>
<td>99</td>
<td>5.8</td>
<td>27</td>
<td>92</td>
<td>46</td>
<td>-44.7*</td>
<td></td>
</tr>
</tbody>
</table>

#### 14.2 Primary Hypercholesterolemia (Heterozygous Familial and Nonfamilial) and Mixed Dyslipidemia

The effects of fenofibrate at a dose equivalent to fenofibric acid delayed-release capsules 135 mg once daily were assessed from four randomized, placebo-controlled, double-blind, parallel-group studies including patients with the following mean baseline lipid values: Total-C 206.9 mg/dL; LDL-C 231.8 mg/dL; HDL-C 52.3 mg/dL; and triglycerides 191.0 mg/dL. Fenofibrate therapy lowered LDL-C, Total-C, and the LDL-C/HDL-C ratio. Fenofibrate therapy also lowered triglycerides and raised HDL-C (Table 5).

### Table 5. Mean Percent Change in Lipid Parameters at End of Treatment

<table>
<thead>
<tr>
<th>Treatment Group</th>
<th>Total-C (mg/dL)</th>
<th>LDL-C (mg/dL)</th>
<th>HDL-C (mg/dL)</th>
<th>TG (mg/dL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pooled Cohort</td>
<td>Mean baseline lipid values (n = 646)</td>
<td>306.9</td>
<td>213.8</td>
<td>52.3</td>
</tr>
<tr>
<td>All Fenofibrate (n = 361)</td>
<td>-10.7%*</td>
<td>-20.8%*</td>
<td>+11.0%*</td>
<td>-28.9%*</td>
</tr>
<tr>
<td>Placebo (n = 285)</td>
<td>-0.4%</td>
<td>-2.2%</td>
<td>+0.7%</td>
<td>+7.7%</td>
</tr>
<tr>
<td>Baseline LDL-C &gt; 160 mg/dL and TG &lt; 150 mg/dL</td>
<td>Mean baseline lipid values (n = 334)</td>
<td>307.7</td>
<td>227.7</td>
<td>58.1</td>
</tr>
<tr>
<td>All Fenofibrate (n = 193)</td>
<td>-24.2%*</td>
<td>-31.4%*</td>
<td>+9.8%*</td>
<td>-23.5%*</td>
</tr>
<tr>
<td>Placebo (n = 141)</td>
<td>+0.2%</td>
<td>-2.2%</td>
<td>+2.6%</td>
<td>+11.7%</td>
</tr>
<tr>
<td>Baseline LDL-C &gt; 160 mg/dL and TG ≥ 150 mg/dL</td>
<td>Mean baseline lipid values (n = 242)</td>
<td>321.8</td>
<td>219.8</td>
<td>46.7</td>
</tr>
<tr>
<td>All Fenofibrate (n = 126)</td>
<td>-16.8%*</td>
<td>-20.1%*</td>
<td>+14.6%*</td>
<td>-35.9%*</td>
</tr>
<tr>
<td>Placebo (n = 116)</td>
<td>-3.0%</td>
<td>-6.6%</td>
<td>+2.3%</td>
<td>+0.9%</td>
</tr>
</tbody>
</table>

*Duration of study treatment was 3 to 6 months

* p < 0.05 vs. Placebo

In a subset of the subjects, measurements of Apo B were conducted. Fenofibrate treatment significantly reduced Apo B from baseline to endpoint as compared with placebo (~25.1% vs. 2.4%, p = 0.0001, n = 231 and 143, respectively).

### 16 HOW SUPPLIED/STORAGE AND HANDLING

Product: 50090-4373

NDC: 50090-4373-0 90 CAPSULE, DELAYED RELEASE in a BOTTLE
17 PATIENT COUNSELING INFORMATION

Patients should be advised:
- of the potential benefits and risks of fenofibric acid delayed-release capsules.
- of medications that should not be taken in combination with fenofibric acid delayed-release capsules.
- to continue to follow an appropriate lipid-modifying diet while taking fenofibric acid delayed-release capsules.
- to take fenofibric acid delayed-release capsules once daily, without regard to food, at the prescribed dose, swallowing each capsule whole.
- to return for routine monitoring.
- to inform their physician of all medications, supplements, and herbal preparations they are taking and any change to their medical condition. Patients should also be advised to inform their physicians prescribing a new medication that they are taking fenofibric acid delayed-release capsules.
- to inform their physician of any muscle pain, tenderness, or weakness; onset of abdominal pain; or any other new symptoms.

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Manufactured for
Lupin Pharmaceuticals, Inc.
Baltimore, Maryland 21202
United States

Manufactured by:
Lupin Limited
Goa - 403 722
INDIA

Revised: June 18, 2018
ID#: 255778

SPL MEDGUIDE
MEDICATION GUIDE

Fenofibric Acid (fen-oh-FYE-brik AS-id)
Delayed-Release Capsules, 45 mg and 135 mg
Rx only

Read this Medication Guide before you start taking fenofibric acid delayed-release capsules and each time you get a refill. There may be new information. This information does not take the place of talking to your healthcare provider about your medical condition or your treatment.

What is the most important information I should know about Fenofibric Acid Delayed-Release Capsules?
Fenofibric acid delayed-release capsules can cause muscle pain, tenderness or weakness, which may be symptoms of a rare but serious muscle condition called rhabdomyolysis. In some cases rhabdomyolysis can cause kidney damage and death. The risk of rhabdomyolysis may be higher when Fenofibric acid delayed-release capsules are given with statins. If you take a statin, tell your healthcare provider.

What are Fenofibric Acid Delayed-Release Capsules?
Fenofibric acid delayed-release capsules are a prescription medicine used to treat cholesterol in the blood by lowering the total amount of triglycerides and LDL (bad) cholesterol, and increasing the HDL (good) cholesterol. Fenofibric acid delayed-release capsules have not been shown to lower your risk of having heart problems or a stroke. You should be on a low fat and low cholesterol diet while you take fenofibric acid delayed-release capsules.

The safety and effectiveness of fenofibric acid delayed-release capsule in children is not known.

Who should not take Fenofibric Acid Delayed-Release Capsules?
Do not take fenofibric acid delayed-release capsules if you:
- are allergic to fenofibric acid, or any of the ingredients in fenofibric acid delayed-release capsules. See the end of this Medication Guide for a list of all the ingredients in fenofibric acid delayed-release capsules.
- have severe kidney disease.
- have liver disease.
- have gallbladder disease.
- are a nursing mother.

Talk to your healthcare provider before you take fenofibric acid delayed-release capsules if you have any of these conditions.

What should I tell my healthcare provider before taking Fenofibric Acid Delayed-Release Capsules?
Before taking fenofibric acid delayed-release capsules, tell your healthcare provider about all your medical conditions, including if you:
- are allergic to any medicines.
- have ever had kidney problem.
- have ever had liver problem.
- have ever had gallbladder problem.
- are pregnant or if you plan to become pregnant. It is not known if fenofibric acid delayed-release capsules will harm your unborn baby.
- are breastfeeding or plan to breastfeed. It is not known if fenofibric acid passes into your breast milk. You and your healthcare provider should decide if you will take fenofibric acid delayed-release capsules or breastfeed. You should not do both.

Tell your healthcare provider about all the medicines you take, including prescription and non-
prescription medicines, vitamins and herbal supplements.

Using fenofibric acid delayed-release capsules with certain other medicines can affect the way these medicines work and other medicines may affect how fenofibric acid delayed-release capsules works. In some cases, using fenofibric acid delayed-release capsules with other medicines can cause serious side effects.

Know all the medicines you take. Keep a list of them and show it to your healthcare provider when you get a new medicine.

It is especially important to tell your healthcare provider if you take any of the medicines listed below:

- anticoagulants, also known as blood thinners (Warfarin, Coumadin)
- bile acid resins
- cyclosporine

Ask your healthcare provider if you are not sure if your medicine is one of these.

How should I take Fenofibric Acid Delayed-Release Capsules?

- You should be on a low fat and low cholesterol diet while you take fenofibric acid delayed-release capsules.
- Take fenofibric acid delayed-release capsules one time each day as prescribed by your healthcare provider.
- Take fenofibric acid delayed-release capsules with or without food.
- Swallow fenofibric acid delayed-release capsules whole. Do not break, crush, dissolve, or chew fenofibric acid delayed-release capsules before swallowing. If you cannot swallow fenofibric acid delayed-release capsules whole, tell your healthcare provider, you may need a different medicine.
- If you miss a dose of fenofibric acid delayed-release capsules, take it as soon as you remember. If it is almost time for your next dose, just skip the missed dose. Take the next dose at your regular time. If you are not sure about your dosing, call your healthcare provider. Do not take more than one dose of fenofibric acid delayed-release capsules a day unless your healthcare provider tells you to.
- If you take too much fenofibric acid delayed-release capsules, contact your healthcare provider or your local emergency department.
- Do not change your dose or stop fenofibric acid delayed-release capsules unless your healthcare provider tells you to.
- Your healthcare provider may do blood tests before you start taking fenofibric acid delayed-release capsules and during treatment. See your healthcare provider regularly to check your cholesterol and triglyceride levels and to check for side effects.

What are the possible side effects with Fenofibric Acid Delayed-Release Capsules?

Fenofibric acid delayed-release capsules may cause serious side effects, including:

- muscle pain, tenderness, or weakness. See "What is the most important information that I should know about fenofibric acid delayed-release capsules?"
- tiredness and fever.
- abdominal pain, nausea, or vomiting. These may be signs of inflammation (swelling) of the gallbladder or pancreas.

Call your healthcare provider right away if you have any of these serious side effects.

The most common side effects with fenofibric acid delayed-release capsules include:

- headache
- heartburn (indigestion)
- nausea
- muscle aches
- increases in muscle or liver enzymes that are measured by blood tests

Tell your healthcare provider if you have any side effect that bothers you or that does not go away. These are not all the possible side effects of fenofibric acid delayed-release capsules. For more information, ask your healthcare provider or pharmacist.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How do I store Fenofibric Acid Delayed-Release Capsules?

- Store fenofibric acid delayed-release capsules between 59 to 86° F (15 to 30° C).
- Protect fenofibric acid delayed-release capsules from moisture.

Keep fenofibric acid delayed-release capsules and all medicines out of the reach of children.

General information about the safe and effective use of Fenofibric Acid Delayed-Release Capsules.

Medicines are sometimes prescribed for conditions that are not mentioned in the Medication Guide. Do not use fenofibric acid delayed-release capsules for a condition for which it was not prescribed. Do not give fenofibric acid delayed-release capsules to other people, even if they have the same condition you have. It may harm them.

This Medication Guide summarizes the most important information about fenofibric acid delayed-release capsules. It may not cover all possible information that is written for health professionals.

For more information go to www.lupinpharmaceuticals.com or call at 1-800-399-2561.

What are the ingredients in Fenofibric Acid Delayed-Release Capsules?

Active Ingredient: Fenofibric acid

Inactive Ingredients: colloidal silicon dioxide, dibutyl sebacate, ethyl cellulose, hypromellose, lactose monohydrate, magnesium stearate, methacrylic acid co polymer, povidone, sodium stearyl fumarate, talc and triethyl citrate. The capsule shell of the 45 mg capsule contains the following inactive ingredients: gelatin, iron oxide black, iron oxide red, iron oxide yellow, sodium lauryl sulphate and titanium dioxide. The capsule shell of the 135 mg capsule contains the following inactive ingredients: FD and C Blue #1, gelatin, iron oxide yellow, sodium lauryl sulphate and titanium dioxide. The capsules are printed with edible ink containing iron oxide black, potassium hydroxide, propylene glycol and shellac.

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Pharmaceuticals, Inc. The makers of these brands are not affiliated with and do not endorse Lupin Pharmaceuticals, Inc. or its products.

Manufactured for
Lupin Pharmaceuticals, Inc.
Baltimore, Maryland 21202
United States

Manufactured by:
Lupin Limited
Goa 403 722
INDIA

Revised: June 15, 2015
ID#: 241784

Storage
Store at 25°C (77°F); excursions permitted to 15 to 30°C (59 to 86°F). [see USP Controlled Room Temperature]. Keep out of the reach of children. Protect from moisture.

Fenofibric acid

FENOFIBRIC ACID
capone, delayed release

Product Information

Product Type: HUMAN PRESCRIPTION DRUG
Item Code (Source): NDC:50090-4373 (NDC:68180-129)
Route of Administration: ORAL

Active Ingredient/Active Moiety

<table>
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<th>Ingredient Name</th>
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<th>Strength</th>
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</thead>
<tbody>
<tr>
<td>CHOLINE FENOFIBRATE (UNII: 4BMH7IZT98)</td>
<td>(FENOFIBRIC ACID - UNII:BGF9MN2HU1)</td>
<td>FENOFIBRIC ACID 135 mg</td>
</tr>
</tbody>
</table>

Inactive Ingredients

<table>
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<tr>
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<th>Strength</th>
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<tr>
<td>DIBUTYL SEBACATE (UNII: 4W5IH7FLNY)</td>
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</tr>
<tr>
<td>ETHYLCELLULOSE, UNSPECIFIED (UNII: 7Z8S9VYZ4B)</td>
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<td>FD&amp;C BLUE NO. 1 (UNII: E477C78JUL)</td>
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<td>FERRIC OXIDE YELLOW (UNII: EX438O2MRT)</td>
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<td>FERROSOFERRIC OXIDE (UNII: XM0M87F357)</td>
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<td>HYPROMELLOSE, UNSPECIFIED (UNII: 3NXW29V3WO)</td>
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<td>METHACRYLIC ACID - ETHYL ACRYLATE COPOLYMER (1:1) TYPE A (UNII: XX7LVST63)</td>
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<td>POTASSIUM HYDROXIDE (UNII: W2EDC948MT)</td>
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<td>Povidone K90 (UNII: RDH86HJV5Z)</td>
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<td>PROPYLENE GLYCOL (UNII: 6DC9Q167V3)</td>
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<tr>
<td>SILICA (UNII: 1-M31H6770)</td>
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<tr>
<td>SILICON DIOXIDE (UNII: EXTSX0004)</td>
<td></td>
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<tr>
<td>SODIUM LAURYL SULFATE (UNII: 368GB5141J)</td>
<td></td>
</tr>
<tr>
<td>SODIUM STEARYL FUMARATE (UNII: 7CV7WJK4UI)</td>
<td></td>
</tr>
<tr>
<td>TALC (UNII: 7SEV7J4R1U)</td>
<td></td>
</tr>
<tr>
<td>TITANIUM DIOXIDE (UNII: 15FIX9V2JP)</td>
<td></td>
</tr>
<tr>
<td>TRISODIUM CITRATE (UNII: 5TINO5GR46)</td>
<td></td>
</tr>
</tbody>
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Product Characteristics

| Color | BLUE (Blue opaque cap), YELLOW (Yellow opaque body) |
| Shape | CAPSULE |
| Flavor | Imprint Code: LU;Q42 |
| Score | no score |
| Size | Units |

Packaging

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<tr>
<th>Item Code</th>
<th>Package Description</th>
<th>Marketing Start Date</th>
<th>Marketing End Date</th>
</tr>
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<tbody>
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<td>NDC:50090-4373-0</td>
<td>90 in 1 BOTTLE</td>
<td>06/20/2019</td>
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Marketing Information

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Labeler - A-S Medication Solutions (E0106420)

Establishment

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