

Name of Medicine

EZETROL[®]

ezetimibe

10 mg tablet

Presentation

EZETROL[®] (ezetimibe) 10 mg is a white to off white capsule shaped tablet debossed with 414 on one side and plain on the other. Dimensions are 8.13 mm x 4.06 mm.

Therapeutic Class

EZETROL (ezetimibe) is in a new class of lipid-lowering compounds that selectively inhibit the intestinal absorption of cholesterol and related plant sterols.

Indications

Primary Hypercholesterolaemia

EZETROL, administered with an HMG-CoA reductase inhibitor (statin) or alone, is indicated as adjunctive therapy to diet for the reduction of elevated total cholesterol (total-C), low-density lipoprotein cholesterol (LDL-C), apolipoprotein B (Apo B), and triglycerides (TG) and to increase high-density lipoprotein cholesterol (HDL-C) in adult and adolescent (10 to 17 years of age) patients with primary (heterozygous familial and non-familial) hypercholesterolaemia.

Homozygous Familial Hypercholesterolaemia (HoFH)

EZETROL, administered with a statin, is indicated for the reduction of elevated total-C and LDL-C levels in adult and adolescent (10 to 17 years of age) patients with HoFH. Patients may also receive adjunctive treatments (e.g., LDL apheresis).

Homozygous Sitosterolaemia (Phytosterolaemia)

EZETROL is indicated for the reduction of elevated sitosterol and campesterol levels in patients with homozygous familial sitosterolaemia.

Dosage and Administration

The patient should be on an appropriate lipid-lowering diet and should continue on this diet during treatment with EZETROL.

The recommended dose of EZETROL is 10 mg once daily, used alone or with a statin. EZETROL can be administered at any time of the day, with or without food.

Use in the Elderly

No dosage adjustment is required for elderly patients (see Pharmacokinetics, *Characteristics in Patients [Special Populations]*).

Use in Paediatric Patients

Children and adolescents ≥ 10 years: No dosage adjustment is required (see Pharmacokinetics, *Characteristics in Patients [Special Populations]*).

Children < 10 years: Treatment with EZETROL is not recommended.

Use in Hepatic Impairment

No dosage adjustment is required in patients with mild hepatic insufficiency (Child Pugh score 5 to 6). Treatment with ezetimibe is not recommended in patients with moderate (Child Pugh score 7 to 9) or severe (Child Pugh score >9) liver dysfunction. (See Warnings and Precautions and Pharmacokinetics, *Characteristics in Patients [Special Populations]*.)

Use in Renal Impairment

No dosage adjustment is required for renally impaired patients (see Pharmacokinetics, *Characteristics in Patients [Special Populations]*).

Co-administration with bile acid sequestrants

Dosing of EZETROL should occur either ≥ 2 hours before or ≥ 4 hours after administration of a bile acid sequestrant.

Contraindications

Hypersensitivity to any component of this medication.

When EZETROL is to be administered with a statin, please refer to the data sheet for that particular statin.

Warnings and Precautions

When EZETROL is to be administered with a statin, please refer to the data sheet for that particular statin.

Liver Enzymes

In controlled co-administration trials in patients receiving EZETROL with a statin, consecutive transaminase elevations (≥ 3 X the upper limit of normal [ULN]) have been observed (See Adverse Effects). When EZETROL is co-administered with a statin, liver function tests should be performed at initiation of therapy and according to the recommendations of the statin, and periodically thereafter. If an increase in ALT or AST ≥ 3 X the ULN persists the statin dose should be reduced or the statin withdrawn.

Skeletal Muscle

In clinical trials, there was no excess of myopathy or rhabdomyolysis associated with EZETROL compared with the relevant control arm (placebo or statin alone). However, myopathy and rhabdomyolysis are known adverse reactions to statins and other lipid-lowering medicines. In clinical trials, the incidence of CPK >10 X ULN was 0.2% for EZETROL vs 0.1% for placebo, and 0.1% for EZETROL co-administered with a statin vs 0.4% for statins alone.

In post-marketing experience with EZETROL, cases of myopathy and rhabdomyolysis have been reported regardless of causality. Most patients who developed rhabdomyolysis were taking a statin prior to initiating EZETROL. However, rhabdomyolysis has been reported very rarely with EZETROL monotherapy and very rarely with the addition of EZETROL to agents known to be associated with increased risk of rhabdomyolysis. All patients starting therapy with EZETROL should be advised of the risk of myopathy and told to report promptly any unexplained muscle pain, tenderness or weakness. EZETROL and any statin that the patient is taking concomitantly should be immediately discontinued if myopathy is diagnosed or suspected. The presence of these symptoms and a creatine phosphokinase (CPK) level >10 times the ULN indicates myopathy.

Hepatic Insufficiency

Due to the unknown effects of the increased exposure to ezetimibe in patients with moderate or severe hepatic insufficiency, EZETROL is not recommended in these patients (see Pharmacokinetics, *Characteristics in Patients [Special Populations]*).

Fibrates

The safety and efficacy of ezetimibe administered with fibrates have not been established; therefore, co-administration of EZETROL and fibrates is not recommended (see Interactions).

Cyclosporine

Caution should be exercised when initiating ezetimibe in the setting of cyclosporine. Cyclosporine concentrations should be monitored in patients receiving EZETROL and cyclosporine (see Interactions).

Anticoagulants

If EZETROL is added to warfarin, another coumarin anticoagulant, or fluindione, the International Normalised Ratio (INR) should be appropriately monitored (see Interactions).

Pregnancy

No clinical data on exposed pregnancies are available. Animal studies of ezetimibe administered alone do not indicate direct or indirect harmful effects with respect to pregnancy, embryonal/foetal development, parturition or postnatal development (see *Development*). However, caution should be exercised when prescribing to pregnant women.

When ezetimibe was given with lovastatin, simvastatin, pravastatin or atorvastatin, no teratogenic effects were observed in embryo-foetal development studies in pregnant rats. In pregnant rabbits, a low incidence of skeletal malformations was observed (see *Development*).

When ezetimibe is to be administered with a statin, please refer to the data sheet for that particular statin.

Nursing Mothers

Studies in rats have shown that ezetimibe is excreted in milk. It is not known whether ezetimibe is excreted into human breast milk, therefore, EZETROL should not be used in nursing mothers unless the potential benefit justifies the potential risk to the infant.

Paediatric Use

Safety and effectiveness of EZETROL co-administered with simvastatin in patients 10 to 17 years of age with heterozygous familial hypercholesterolaemia have been evaluated in a controlled clinical trial in adolescent boys and in girls who were at least one year post-menarche. Adolescent patients treated with EZETROL and up to 40 mg/day simvastatin had an adverse experience profile similar to that of adult patients treated with EZETROL and simvastatin. However, elevations of CPK ($\geq 10 \times \text{ULN}$) occurred in two patients (2%) treated with EZETROL co-administered with simvastatin and in zero patients treated with simvastatin alone. No cases of myopathy were reported. In this controlled study, there was no detectable effect on growth or sexual maturation in the adolescent boys or girls, or any effect on menstrual cycle length in girls. (See Dosage and Administration and Adverse Effects.) EZETROL has not been studied in patients younger than 10 years of age or in pre-menarchal girls.

Animal Pharmacology

The hypocholesterolaemic effect of ezetimibe was evaluated in Rhesus monkeys, a model for the human metabolism of cholesterol, as well as in dogs. Rhesus monkeys were fed a cholesterol-containing diet that mimics a human Western diet. Ezetimibe was found to have an ED₅₀ of 0.0005 mg/kg/day for inhibiting the rise in plasma cholesterol levels (ED₁₀₀ = 0.003 mg/kg/day). The ED₅₀ in dogs was found to be 0.007 mg/kg/day. These results are consistent with EZETROL being an extremely potent cholesterol absorption inhibitor.

In dogs given ezetimibe (≥ 0.03 mg/kg/day), the concentration of cholesterol in gallbladder bile increased ~2- to 3-fold. However, a dose of 300 mg/kg/day administered to dogs for one year did not result in gallstone formation or any other adverse hepatobiliary effects. In mice given ezetimibe (0.3 to 5 mg/kg/day) and fed a normal or cholesterol rich diet, the concentration of cholesterol in gallbladder bile was either unaffected or reduced to normal levels, respectively. The relevance of these preclinical findings to humans is unknown.

Animal Toxicology

Acute Toxicity

In animals, no toxicity was observed after single oral doses of 5000 mg/kg of ezetimibe in rats and mice and 3000 mg/kg in dogs.

Chronic Toxicity

Ezetimibe was well tolerated by mice, rats and dogs. No target organs of toxicity were identified in chronic studies at daily doses up to 1500 (males) and 500 mg/kg (females) in rats, up to 500 mg/kg in mice, or up to 300 mg/kg in dogs.

The safety of concomitant administration of ezetimibe and statins was assessed in rats and dogs. When ezetimibe was co-administered with atorvastatin, simvastatin, pravastatin or lovastatin, for three months, toxicologic findings were consistent with those seen with statins administered alone.

Carcinogenicity

In two-year studies conducted in mice and rats, ezetimibe was not carcinogenic.

Mutagenesis

Ezetimibe was not genotoxic in a series of *in vivo* and *in vitro* tests.

Combinations of ezetimibe with atorvastatin, simvastatin, pravastatin, or lovastatin were not genotoxic in a series of *in vitro* and *in vivo* assays.

Reproduction

Ezetimibe did not affect the fertility of male or female rats.

Development

Ezetimibe was not teratogenic in rats or rabbits and had no effect on prenatal or postnatal development.

Concomitant administration of ezetimibe and statins was not teratogenic in rats. In pregnant rabbits, a low incidence of skeletal malformations (fused sternbrae, fused caudal vertebrae, reduced number of caudal vertebrae) was observed when ezetimibe (1000 mg/kg; ≥ 146 times the human exposure at 10 mg daily based on AUC_{0-24hr} for total ezetimibe) was administered with lovastatin (2.5 and 25 mg/kg), simvastatin (5 and 10 mg/kg), pravastatin (25 and 50 mg/kg), or atorvastatin (5, 25, and 50 mg/kg). Exposure to the pharmacologically active form of the statin ranged from 1.4 (atorvastatin) to 547

(lovastatin) times the human exposure at 10 mg daily (simvastatin or atorvastatin) or 20 mg daily (lovastatin and pravastatin) based on AUC_{0-24hr} .

Effects on Ability to Use and Drive Machinery

No studies of the effects on the ability to drive and use of machines have been performed. However, certain side effects that have been reported with EZETROL may affect some patients' ability to drive or operate machinery. Individual responses to EZETROL may vary. (See Adverse Effects.)

Adverse Effects

Clinical studies of up to 112 weeks duration in which EZETROL 10 mg daily was administered alone (n=2396), or with a statin (n=11,308), patients demonstrated: EZETROL was generally well tolerated, adverse reactions were usually mild and transient, the overall incidence of side effects reported with EZETROL was similar to that reported with placebo, and the discontinuation rate due to adverse experiences was comparable between EZETROL and placebo.

The following common ($\geq 1/100$, $< 1/10$) or uncommon ($\geq 1/1,000$, $< 1/100$); medicine-related adverse experiences were reported in patients taking EZETROL alone (n = 2396) and at a greater incidence than placebo (n=1159), or in patients taking EZETROL co-administered with a statin (n = 11,308) and at a greater incidence than statin administered alone (n=9361):

EZETROL administered alone:

Investigations:

Uncommon: ALT and/or AST increased; blood CPK increased; gamma-glutamyltransferase increased; liver function test abnormal

Respiratory, Thoracic and Mediastinal Disorders:

Uncommon: cough

Gastrointestinal Disorders:

Common: abdominal pain; diarrhoea; flatulence

Uncommon: dyspepsia; gastroesophageal reflux disease; nausea

Musculoskeletal and Connective Tissue Disorders

Uncommon: arthralgia; muscle spasms; neck pain

Metabolism and Nutrition Disorders:

Uncommon: decreased appetite

Vascular Disorders:

Uncommon: hot flush; hypertension

General Disorders and Administration Site Condition:

Common: fatigue

Uncommon: chest pain; pain

EZETROL co-administered with a statin:

Investigations:

Common: ALT and/or AST increased

Nervous System Disorders:

Common: headache

Uncommon: paresthesia

Gastrointestinal Disorders:

Uncommon: dry mouth; gastritis

Skin and Subcutaneous Tissue Disorders:

Uncommon: pruritus; rash; urticaria

Musculoskeletal and Connective Tissue Disorders:

Common: myalgia

Uncommon: back pain; muscular weakness; pain in extremity

General Disorders and Administration Site Condition:

Uncommon: asthenia; oedema peripheral

In a study involving adolescent (10 to 17 years of age) patients with heterozygous familial hypercholesterolaemia (n = 248), the safety and tolerability profile of the group co-administered EZETROL and simvastatin was similar to that of adult patients co-administered EZETROL and simvastatin (see Warnings and Precautions, *Paediatric Use*).

Laboratory Test Findings

In controlled clinical monotherapy trials, the incidence of clinically important elevations in serum transaminases (ALT and/or AST ≥ 3 X ULN, consecutive) was similar between EZETROL (0.5 %) and placebo (0.3 %). In co-administration trials, the incidence was 1.3% for patients treated with EZETROL co-administered with a statin and 0.4% for patients treated with a statin alone. These elevations were generally asymptomatic, not associated with cholestasis, and returned to baseline after discontinuation of therapy or with continued treatment (See Warnings and Precautions).

Clinically important elevations of CPK (≥ 10 X ULN) in patients treated with EZETROL administered alone or co-administered with a statin were similar to elevations seen with placebo or statin administered alone, respectively.

In a study involving adolescent (10 to 17 years of age) patients with heterozygous familial hypercholesterolaemia (n = 248), elevations of CPK (≥ 10 X ULN) occurred in two patients (2%) treated with EZETROL plus simvastatin and in zero patients treated with simvastatin alone. No cases of myopathy were reported.

Post-Marketing Experience

The following adverse reactions have been reported in post-marketing experience, regardless of causality assessment:

Blood and lymphatic system disorders: thrombocytopaenia

Nervous system disorders: dizziness; paraesthesia

Gastrointestinal disorders: pancreatitis; constipation

Skin and subcutaneous tissue disorders: erythema multiforme

Musculoskeletal and connective tissue disorders: myalgia; myopathy/rhabdomyolysis (See Warnings and Precautions)

General disorders and administration site conditions: asthenia

Immune system disorders: Hypersensitivity reactions, including anaphylaxis, angioedema, rash, and urticaria

Hepatobiliary disorders: hepatitis; cholelithiasis; cholecystitis

Psychiatric disorders: depression

Interactions

In preclinical studies, it has been shown that ezetimibe does not induce cytochrome P450 medicine metabolising enzymes. No clinically significant pharmacokinetic interactions have been observed between ezetimibe and medicines known to be metabolised by cytochromes P450 1A2, 2D6, 2C8, 2C9, and 3A4, or N-acetyltransferase.

Ezetimibe had no effect on the pharmacokinetics of dapsone, dextromethorphan, digoxin, oral contraceptives (ethinyl estradiol and levonorgestrel), glipizide, tolbutamide, or midazolam during co-administration. Cimetidine, co-administered with ezetimibe, had no effect on the bioavailability of ezetimibe.

Antacids: Concomitant antacid administration decreased the rate of absorption of ezetimibe but had no effect on the bioavailability of ezetimibe. This decreased rate of absorption is not considered clinically significant.

Cholestyramine: Concomitant cholestyramine administration decreased the mean AUC of total ezetimibe (ezetimibe + ezetimibe glucuronide) approximately 55 %. The incremental LDL-C reduction due to adding ezetimibe to cholestyramine may be lessened by this interaction.

Cyclosporine: In a study of eight post-renal transplant patients with creatinine clearance of >50 mL/min on a stable dose of cyclosporine, a single 10 mg dose of ezetimibe resulted in a 3.4-fold (range 2.3- to 7.9-fold) increase in the mean AUC for total ezetimibe compared to a healthy control population from another study (n=17). In a different study, a renal transplant patient with severe renal insufficiency (creatinine clearance of 13.2 mL/min/1.73 m²) who was receiving multiple medications, including cyclosporine, demonstrated a 12-fold greater exposure to total ezetimibe compared to concurrent controls. In a two-period crossover study in twelve healthy subjects, daily administration of 20 mg ezetimibe for 8 days with a single 100 mg dose of cyclosporine on Day 7 resulted in a mean 15% increase in cyclosporine AUC (range 10% decrease to 51% increase) compared to a single 100 mg dose of cyclosporine alone (see Warnings and Precautions).

Fibrates: Concomitant fenofibrate or gemfibrozil administration increased total ezetimibe concentrations approximately 1.5- and 1.7-fold respectively, however these increases are not considered clinically significant. The safety and effectiveness of ezetimibe administered with fibrates have not been established. Fibrates may increase cholesterol excretion into the bile, leading to cholelithiasis. In a preclinical study in dogs, ezetimibe increased cholesterol in the gallbladder bile (see Animal Pharmacology). Although the relevance of this preclinical finding to humans is unknown, coadministration of EZETROL with fibrates is not recommended until use in patients is studied.

Statins: No clinically significant pharmacokinetic interactions were seen when ezetimibe was co-administered with atorvastatin, simvastatin, pravastatin, lovastatin, fluvastatin, or rosuvastatin.

Anticoagulants: Concomitant administration of ezetimibe (10 mg once daily) had no significant effect on bioavailability of warfarin and prothrombin time in a study of twelve healthy adult males. There have been post-marketing reports of increased International Normalised Ratio in patients who had EZETROL added to warfarin or fluindione. Most of these patients were also on other medications (See Warnings and Precautions).

Overdosage

In clinical studies, administration of ezetimibe, 50 mg/day to 15 healthy subjects for up to 14 days, 40 mg/day to 18 patients with primary hypercholesterolaemia for up to 56 days,

and 40 mg/day to 27 patients with homozygous sitosterolaemia for 26 weeks, was generally well tolerated.

A few cases of over dosage with ezetimibe have been reported; most have not been associated with adverse experiences. Reported adverse experiences have not been serious. In the event of an overdose, symptomatic and supportive measures should be employed.

Actions

EZETROL is orally active and potent, with a unique mechanism of action that differs from other classes of cholesterol-reducing compounds (e.g., statins, bile acid sequestrants [resins], fibric acid derivatives, and plant stanols). The molecular target of ezetimibe is the sterol transporter, Niemann-Pick C1-Like 1 (NPC1L1), which is responsible for the intestinal uptake of cholesterol and phytosterols.

Ezetimibe localises at the brush border of the small intestine and inhibits the absorption of cholesterol, leading to a decrease in the delivery of intestinal cholesterol to the liver. This causes a reduction of hepatic cholesterol stores and an increase in clearance of cholesterol from the blood. Ezetimibe does not increase bile acid excretion (like bile acid sequestrants) and does not inhibit cholesterol synthesis in the liver (like statins).

In a 2-week clinical study in 18 hypercholesterolaemic patients, EZETROL inhibited intestinal cholesterol absorption by 54 %, compared with placebo. By inhibiting the absorption of intestinal cholesterol, ezetimibe reduces the delivery of cholesterol to the liver. Statins reduce cholesterol synthesis in the liver. Together these distinct mechanisms provide complementary cholesterol reduction. EZETROL, administered with a statin, reduces total-C, LDL-C, Apo B, and TG and increases HDL C in patients with hypercholesterolaemia, beyond either treatment alone.

Clinical studies demonstrate that elevated levels of total-C, LDL-C and Apo B, the major protein constituent of LDL, promote human atherosclerosis. In addition, decreased levels of HDL-C are associated with the development of atherosclerosis. Epidemiologic studies have established that cardiovascular morbidity and mortality vary directly with the level of total-C and LDL-C and inversely with the level of HDL-C. Like LDL, cholesterol-enriched triglyceride-rich lipoproteins, including very-low-density lipoproteins (VLDL), intermediate-density lipoproteins (IDL), and remnants, can also promote atherosclerosis.

A series of preclinical studies was performed to determine the selectivity of ezetimibe for inhibiting cholesterol absorption. Ezetimibe inhibited the absorption of [¹⁴C]-cholesterol with no effect on the absorption of triglycerides, fatty acids, bile acids, progesterone, ethinyl estradiol, or the fat soluble vitamins A and D.

Pharmacokinetics

Absorption

After oral administration, ezetimibe is rapidly absorbed and extensively conjugated to a pharmacologically active phenolic glucuronide (ezetimibe-glucuronide). Mean maximum plasma concentrations (C_{max}) occur within 1 to 2 hours for ezetimibe-glucuronide and 4 to 12 hours for ezetimibe. The absolute bioavailability of ezetimibe cannot be determined as the compound is virtually insoluble in aqueous media suitable for injection.

Concomitant food administration (high fat or non-fat meals) had no effect on the oral

bioavailability of ezetimibe when administered as EZETROL 10 mg tablets. EZETROL can be administered with or without food.

Distribution

Ezetimibe and ezetimibe-glucuronide are bound 99.7% and 88 to 92% to human plasma proteins, respectively.

Metabolism

Ezetimibe is metabolised primarily in the small intestine and liver via glucuronide conjugation (a phase II reaction) with subsequent biliary excretion. Minimal oxidative metabolism (a phase I reaction) has been observed in all species evaluated. Ezetimibe and ezetimibe-glucuronide are the major medicine-derived compounds detected in plasma, constituting approximately 10 to 20 % and 80 to 90 % of the total medicine in plasma, respectively. Both ezetimibe and ezetimibe-glucuronide are slowly eliminated from plasma with evidence of significant enterohepatic recycling. The half-life for ezetimibe and ezetimibe-glucuronide is approximately 22 hours.

Elimination

Following oral administration of ¹⁴C-ezetimibe (20 mg) to human subjects, total ezetimibe accounted for approximately 93 % of the total radioactivity in plasma. Approximately 78 % and 11 % of the administered radioactivity were recovered in the faeces and urine, respectively, over a 10-day collection period. After 48 hours, there were no detectable levels of radioactivity in the plasma.

Characteristics in Patients (Special Populations)

Paediatric Patients

The absorption and metabolism of ezetimibe are similar between children and adolescents (10 to 18 years) and adults. Based on total ezetimibe, there are no pharmacokinetic differences between adolescents and adults. Pharmacokinetic data in the paediatric population <10 years of age are not available.

Geriatric Patients

Plasma concentrations for total ezetimibe are about 2-fold higher in the elderly (≥65 years) than in the young (18 to 45 years). LDLC reduction and safety profile are comparable between elderly and young subjects treated with EZETROL. Therefore, no dosage adjustment is necessary in the elderly.

Hepatic Insufficiency

After a single 10 mg dose of ezetimibe, the mean area under the curve (AUC) for total ezetimibe was increased approximately 1.7-fold in patients with mild hepatic insufficiency (Child Pugh score 5 or 6), compared to healthy subjects. In a 14-day, multiple-dose study (10 mg daily) in patients with moderate hepatic insufficiency (Child Pugh score 7 to 9), the mean AUC for total ezetimibe was increased approximately 4-fold on Day 1 and Day 14 compared to healthy subjects. No dosage adjustment is necessary for patients with mild hepatic insufficiency. Due to the unknown effects of the increased exposure to ezetimibe in patients with moderate or severe (Child Pugh score >9) hepatic insufficiency, ezetimibe is not recommended in these patients (see Warnings and Precautions).

Renal Insufficiency

After a single 10 mg dose of ezetimibe in patients with severe renal disease (n=8; mean CrCl ≤30 mL/min/1.73m²), the mean AUC for total ezetimibe was increased approximately 1.5-fold, compared to healthy subjects (n=9). This result is not considered clinically significant. No dosage adjustment is necessary for renally impaired patients.

An additional patient in this study (post-renal transplant and receiving multiple medications, including cyclosporine) had a 12-fold greater exposure to total ezetimibe.

Gender

Plasma concentrations for total ezetimibe are slightly higher (<20 %) in women than in men. LDL-C reduction and safety profile are comparable between men and women treated with ezetimibe. Therefore, no dosage adjustment is necessary on the basis of gender.

Race

Based on a meta-analysis of pharmacokinetic studies, there were no pharmacokinetic differences between Blacks and Caucasians.

Pharmaceutical Precautions

Store below 30°C. Store in the original package.

Medicine Classification

Prescription Medicine

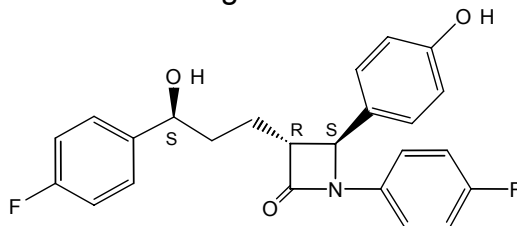
Package Quantities

EZETROL 10 mg, tablets are available in packs of 30.

Further Information

Chemistry

EZETROL, ezetimibe is described chemically as 1-(4-fluorophenyl)-3(R)-[3-(4-fluorophenyl)-3(S)-hydroxypropyl]-4(S)-(4-hydroxyphenyl)-2-azetidinone. The empirical formula is $C_{24}H_{21}F_2NO_3$. Its molecular weight is 409.4 and its structural formula is:



Ezetimibe is a white, crystalline powder that is freely to very soluble in ethanol, methanol, and acetone and practically insoluble in water. Ezetimibe has a melting point of about 163°C and is stable at ambient temperature.

Composition

Active Ingredient

Each tablet of EZETROL for oral administration contains 10 mg ezetimibe.

Inactive Ingredients

Each 10 mg tablet contains croscarmellose sodium, lactose monohydrate, magnesium stearate, microcrystalline cellulose, povidone, and sodium laurilsulfate.

Name and Address

Merck Sharp & Dohme (New Zealand) Limited
P O Box 99 851
Newmarket
Auckland
NEW ZEALAND
Tel: 0800 500 673

Date of Preparation

29 October 2009

DP-EZE-1009(291009)

®Registered Trademark of MSP Singapore Company LLC
Copyright © MSP Singapore Company, LLC, 2008. All rights reserved.