Pitalo® (Pitavastatin) Tablets 1mg 2mg 4mg

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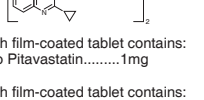
DRUG DESCRIPTION:
PITALO (Pitavastatin) is an inhibitor of HMG-CoA reductase. It is a synthetic lipid-lowering agent for oral administration. The empirical formula for Pitavastatin is $C_{50}H_{46}CaF_2N_2O_8$ and the molecular weight is 880.98.

The structural formula is:



COMPOSITION:
Pitalo® 1mg Tablets: Each film-coated tablet contains: Pitavastatin Calcium eq. to Pitavastatin.....1mg
Genix Specs.
Pitalo® 2mg Tablets: Each film-coated tablet contains: Pitavastatin Calcium eq. to Pitavastatin.....2mg
Genix Specs.
Pitalo® 4mg Tablets: Each film-coated tablet contains: Pitavastatin Calcium eq. to Pitavastatin.....4mg
Genix Specs.

CLINICAL PHARMACOLOGY
Mechanism of Action: Pitavastatin competitively inhibits HMG-CoA reductase, which is a rate-determining enzyme involved with biosynthesis of cholesterol, in a manner of competition with the substrate so that it inhibits cholesterol synthesis in the liver. As a result, the expression of LDL-receptors followed by the uptake of LDL from blood to liver is accelerated and then the plasma TC decreases. Further, the sustained inhibition of cholesterol synthesis in the liver decreases levels of very low density lipoproteins.
Pharmacodynamics: In a randomized, double-blind, placebo-controlled, 4-way parallel, active-comparator study with moxifloxacin in 174 healthy participants, Pitavastatin was not associated with clinically meaningful prolongation of the QTc interval or heart rate at daily doses up to 16 mg (4 times the recommended maximum daily dose). **Pharmacokinetics: Absorption:** Pitavastatin peak plasma concentrations are achieved about 1 hour after oral administration. Both Cmax and AUC increased in an approximately dose-proportional manner for single Pitavastatin doses from 1mg to 4mg once daily. The absolute bioavailability of Pitavastatin oral solution is 51%. Administration of Pitavastatin with a high fat meal (50% fat content) decreases Pitavastatin Cmax by 43% but does not significantly reduce Pitavastatin AUC. The Cmax and AUC of Pitavastatin did not differ following evening or morning drug administration. In healthy volunteers receiving 4 mg Pitavastatin, the percent change from baseline for LDL-C following evening dosing was slightly greater than that following morning dosing. Pitavastatin was absorbed in the small intestine but very little in the colon. **Distribution:** Pitavastatin is more than 99% protein bound in human plasma, mainly to albumin and alpha 1-acid glycoprotein, and the mean volume of distribution is approximately 148 L. Association of Pitavastatin and/or its metabolites with the blood cells is minimal. **Metabolism:** Pitavastatin is marginally metabolized by CYP2C9 and to a lesser extent by CYP2C8. The major metabolite in human plasma is the lactone which is formed via an ester-type Pitavastatin glucuronide conjugate by uridine 5'-diphosphate (UDP) glucuronosyltransferase (UGT1A3 and UGT2B7). **Excretion:** A mean of 15% of radioactivity of orally administered single 32 mg 14C-labeled Pitavastatin dose was excreted in urine, whereas a mean of 79% of the dose was excreted in feces within 7 days. The mean plasma elimination half-life is approximately 12 hours.

INDICATIONS:
Drug therapy should be one component of multiple-risk-factor intervention in individuals who require modifications of their lipid profile. Lipid-altering agents should be used in addition to a diet restricted in saturated fat and cholesterol only when the response to diet & other nonpharmacological measures has been inadequate.
Primary Hyperlipidemia and Mixed Dyslipidemia: PITALO is indicated as an adjunctive therapy to diet to reduce elevated total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), apolipoprotein B (Apo B), triglycerides (TG), and to increase HDL-C in adult patients with primary hyperlipidemia or mixed dyslipidemia.
Limitations of Use: Doses of Pitavastatin greater than 4 mg once daily were associated with an increased risk for severe myopathy in premarketing clinical studies. Do not exceed 4 mg once daily dosing of Pitavastatin.
The effect of Pitavastatin on cardiovascular morbidity and mortality has not been determined. Pitavastatin has not been studied in patients with severe renal impairment (glomerular filtration rate < 30 mL/min/1.73 m2) not on hemodialysis. Pitavastatin should not be used in this patient population.

DOSAGE AND ADMINISTRATION
General Dosing Information: The dose range for PITALO is 1 to 4 mg orally once daily at any time of the day with or without food. The recommended starting dose is 2 mg and the maximum dose is 4 mg. The starting dose and maintenance doses of PITALO should be individualized according to patient characteristics, such as goal of therapy and response. After initiation or upon titration of PITALO, lipid levels should be analyzed after 4 weeks and the dosage adjusted accordingly.**Dosage in Patients with Renal Impairment:** Patients with moderate renal impairment (glomerular filtration rate 30 to < 60 mL/min/1.73 m2) and end -stage renal disease receiving hemodialysis should receive a starting dose of Pitavastatin 1 mg once daily and a maximum dose of Pitavastatin 2 mg once daily. Pitavastatin should not be used in patients with severe renal impairment (glomerular filtration rate < 30 mL/min/1.73 m2)

SIDE EFFECTS:
The following serious adverse reactions are:
• Rhabdomyolysis with myoglobinuria and acute renal failure and myopathy (including myositis).
• Liver Enzyme Abnormalities.
Clinical Studies Experience: Adverse reactions reported in ≥ 2% of patients in controlled clinical studies and at a rate greater than or equal to placebo are shown below. These studies had treatment duration of up to 12 weeks.
Adverse Reactions* Reported by ≥ 2.0% of Patients Treated with Pitavastatin and > Placebo in Short-Term Controlled Studies.

Adverse Reactions*	Placebo N= 208	Pitavastatin 1 mg N=309	Pitavastatin 2 mg N=951	Pitavastatin 4 mg N=1540
Back Pain	2.9%	3.9%	1.8%	1.4%
Constipation	1.9%	3.6%	1.5%	2.2%
Diarrhea	1.9%	2.6%	1.5%	1.9 %
Myalgia	1.4%	1.9%	2.8%	3.1%
Pain in Extremity	1.9%	2.3%	0.6%	0.9%

* Adverse reactions by MedDRA preferred term.

Other adverse reactions reported from clinical studies

were arthralgia, headache, influenza, and nasopharyngitis. The following laboratory abnormalities have also been reported: elevated creatine phosphokinase, transaminases, alkaline phosphatase, bilirubin, and glucose. Hypersensitivity reactions including rash, pruritus, & urticaria have been reported with Pitavastatin.

DRUG INTERACTIONS

Cyclosporine: Cyclosporine significantly increased Pitavastatin exposure. Co-administration of cyclosporine with Pitavastatin is contraindicated. **Lopinavir/Ritonavir:** Based on data with another HMG-CoA reductase inhibitor that has a similar pharmacokinetic profile to that of Pitavastatin, Co-administration of the protease inhibitor combination, lopinavir/ritonavir, with Pitavastatin may significantly increase Pitavastatin exposure. Therefore, Pitavastatin should not be used with this combination of protease inhibitors. **Erythromycin:** Erythromycin significantly increased Pitavastatin exposure. In patients taking erythromycin, a dose of Pitavastatin 1 mg once daily should not be exceeded. **Rifampin:** Rifampin significantly increased Pitavastatin exposure. In patients taking rifampin, a dose of Pitavastatin 2 mg once daily should not be exceeded. **Fibrates:** Because it is known that the risk of myopathy during treatment with HMG-CoA reductase inhibitors may be increased with concurrent administration of fibrates, Pitavastatin should be administered with caution when used concomitantly with gemfibrozil or other fibrates. **Niacin:** The risk of skeletal muscle effects may be enhanced when Pitavastatin is used in combination with niacin; a reduction in Pitavastatin dosage should be considered in this setting **Warfarin:** Pitavastatin had no significant pharmacokinetic interaction with R- and S- warfarin. Pitavastatin had no significant effect on prothrombin time (PT) and international normalized ratio (INR) when administered to patients receiving chronic warfarin treatment. However, patients receiving warfarin should have their PT and INR monitored when Pitavastatin is added to their therapy.

PRECAUTIONS

Skeletal Muscle Effects: Cases of myopathy and rhabdomyolysis with acute renal failure secondary to myoglobinuria have been reported with HMG-CoA reductase inhibitors, including Pitavastatin. These risks can occur at any dose level, but increase in a dose-dependent manner. Pitavastatin should be prescribed with caution in patients with predisposing factors for myopathy. These factors include advanced age (> 65 years), renal impairment, and inadequately treated hypothyroidism. The risk of myopathy may also be increased with concurrent administration of fibrates or lipid-modifying doses of niacin. Pitavastatin should be administered with caution in patients with impaired renal function, in elderly patients, or when used concomitantly with fibrates or lipid-modifying doses of niacin. Pitavastatin therapy should be discontinued if markedly elevated creatine kinase (CK) levels occur or myopathy is diagnosed or suspected. Pitavastatin therapy should also be temporarily withheld in any patient with an acute, serious condition suggestive of myopathy or predisposing to the development of renal failure secondary to rhabdomyolysis (e.g., sepsis, hypotension, dehydration, major surgery, trauma, severe metabolic, endocrine, and electrolyte disorders, or uncontrolled seizures). All patients should be advised to promptly report unexplained muscle pain, tenderness, or weakness, particularly if accompanied by malaise or fever.

Liver Enzyme Abnormalities and Monitoring: Increases in serum transaminases (aspartate aminotransferase [AST]/serum glutamic-oxaloacetic transaminase, or alanine aminotransferase [ALT]/serum glutamic-pyruvic transaminase) have been reported with HMG-CoA reductase inhibitors, including Pitavastatin.

In most cases, the elevations were transient and resolved or improved on continued therapy or after a brief interruption in therapy. It is recommended that liver enzyme tests be performed before and at 12 weeks following both the initiation of therapy and any elevation of dose and periodically (e.g., semiannually) thereafter. Patients who develop increased transaminase levels should be monitored until the abnormalities have resolved. Should an increase in ALT or AST of > 3 times upper limit of normal persist, reduction of dose or withdrawal of Pitavastatin is recommended. As with other HMG-CoA reductase inhibitors, Pitavastatin should be used with caution in patients who consume substantial quantities of alcohol. Active liver disease, which may include unexplained persistent transaminase elevations, is a contraindication to the use of Pitavastatin.

USE IN SPECIFIC POPULATIONS

Pregnancy: Teratogenic effects: Pregnancy Category X Pitavastatin is contraindicated in women who are or may become pregnant. **Nursing Mothers:** It is not known whether Pitavastatin is excreted in human milk, however, it has been shown that a small amount of another drug in this class passes into human milk. Rat studies have shown that Pitavastatin is excreted into breast milk. **Pediatric Use:** Safety and effectiveness of Pitavastatin in pediatric patients have not been established. **Renal Impairment:** Patients with moderate renal impairment (glomerular filtration rate 30 to < 60 mL/min/1.73 m2) and end-stage renal disease receiving hemodialysis should receive a starting dose of Pitavastatin 1 mg once daily and a maximum dose of Pitavastatin 2 mg once daily. **Hepatic Impairment:** Pitavastatin is contraindicated in patients with active liver disease which may include unexplained persistent elevations of hepatic transaminase levels.

INSTRUCTIONS:

Dosage as directed by the physician.
Store at 25°C, excursions permitted
to 15°C - 30°C.
Protect from sunlight and moisture.
Keep all medicines out of the reach of children.
To be sold on the prescription of a registered
medical practitioner only.

PRESENTATION: PITALO® (Pitavastatin) tablets 1mg, 2mg & 4mg film-coated tablets available in Alu-Alu blister pack of 10's with leaflet.

ہدایات:

خوراک ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔

۲۵ ڈگری سینٹی گریڈ پر رکھیں، محفوظ رکھنے کی حد ۱۵ سے ۳۰ ڈگری سینٹی گریڈ ہے۔

سورج کی روشنی اور نمی سے محفوظ رکھیں۔ تمام دوائیں بچوں کی پہنچ سے دور رکھیں۔

صرف رجسٹرڈ ڈاکٹر کے نسخہ پر فروخت کریں۔

For detailed information
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