

ROSUVASTATIN CALCIUM

ROSALTA

10 mg Film-Coated Tablet
ANTHYPERCHOLESTEROLEMIA / ANTIDYSLIPIDAEMIA



FORMULATION:

Each film-coated tablet contains:
Rosuvastatin (as calcium)
Eq. to Rosuvastatin 10 mg

PRODUCT DESCRIPTION:

Light pink, circular, slightly biconvex film coated tablet plain on both the sides.

PHARMACOLOGICAL ACTION:

Rosuvastatin is a selective and competitive inhibitor of HMG-CoA reductase, the rate-limiting enzyme that converts 3-hydroxy-3-methylglutaryl coenzyme A to mevalonate, a precursor of cholesterol (total C), LDL-C, ApoB, and nonHDL-C (total cholesterol minus HDL-C) in patients with homozygous and heterozygous familial hypercholesterolemia, nonfamilial forms of hypercholesterolemia, and mixed dyslipidemia. Rosuvastatin also reduces TG and increases HDL-C. Rosuvastatin reduces total-C, LDL-C, VLDL-cholesterol (VLDL-C), ApoB, nonHDL-C and TG, and increases HDL-C in patients with isolated hypertriglyceridemia. The effect of Rosuvastatin on cardiovascular morbidity and mortality has not been determined.

PHARMACODYNAMIC PROPERTIES:

Pharmacotherapeutic group: HMG-CoA reductase inhibitors

Mechanism of action

Rosuvastatin is a selective and competitive inhibitor of HMG-CoA reductase, the rate-limiting enzyme that converts 3-hydroxy-3-methylglutaryl coenzyme A to mevalonate, a precursor for cholesterol. The primary site of action of Rosuvastatin is the liver, the target organ for cholesterol lowering. Rosuvastatin increases the number of hepatic LDL receptors on the cell-surface, enhancing uptake and catabolism of LDL and it inhibits the hepatic synthesis of VLDL, thereby reducing the total number of VLDL and LDL particles.

PHARMACOKINETICS:

Absorption: The absolute bioavailability of Rosuvastatin is approximately 20%. Plasma concentrations of Rosuvastatin do not differ following evening or morning drug administration. Significant LDL-C reductions are seen when Rosuvastatin is given with or without food, and regardless of the time of day of drug administration.

Distribution: Mean volume of distribution at steady-state of Rosuvastatin is approximately 134 liters. Rosuvastatin is 88% bound to plasma proteins. This binding is reversible and independent of plasma concentrations.

Metabolism: Rosuvastatin is not extensively metabolized, approximately 10% of a radio labeled dose is recovered as metabolite. The major metabolite is N-desmethyl Rosuvastatin, which is formed principally by cytochrome P450 2C9, and *in vitro* studies have demonstrated that N-desmethyl Rosuvastatin has approximately one-sixth to one-half the HMG-CoA reductase inhibitory activity of Rosuvastatin.

Excretion: Following oral administration, Rosuvastatin and its metabolites are primarily excreted in the feces (90%). The elimination half-life of Rosuvastatin is approximately 19 hours.

INDICATIONS:

Hyperlipidemia and Mixed Dyslipidemia

Rosuvastatin Calcium is indicated as adjunctive therapy to diet to reduce elevated Total-C, LDL-C, ApoB, non HDL-C, and triglycerides and to increase HDL-C in adult patients

with primary hyperlipidemia or mixed dyslipidemia. Lipid-altering agents should be used in addition to a diet restricted in saturated fat and cholesterol when response to diet and nonpharmacological interventions alone has been inadequate.

Pediatric Patients 10 to 17 years of age with Heterozygous Familial Hypercholesterolemia (HeFH)

Adjunct on diet to reduce Total-C, LDL-C and ApoB levels in adolescent boys and girls, who are at least one year post menarche, 10-17 years of age with heterozygous familial hypercholesterolemia if after an adequate trial of diet therapy the following findings are present: LDL-C > 190 mg/dL or > 160 mg/dL and there is a positive family history of premature cardiovascular disease (CVD) or two or more other CVD risk factors.

Hypertriglyceridemia

Rosuvastatin Calcium is indicated as adjunctive therapy to diet for the treatment of adult patients with hypertriglyceridemia.

Primary Dysbetalipoproteinemia (Type III Hyperlipoproteinemia)

Rosuvastatin Calcium is indicated as an adjunct to diet for the treatment of patients with primary dysbetalipoproteinemia (Type III hyperlipoproteinemia).

Homozygous Familial Hypercholesterolemia

Rosuvastatin Calcium is indicated as adjunctive therapy to other lipid-lowering treatments (e.g. LDL apheresis) or alone if such treatments are unavailable to reduce LDL-C, Total-C, and ApoB in adult patients with homozygous familial hypercholesterolemia.

Slowing of the Progression of Atherosclerosis

Rosuvastatin Calcium is indicated as adjunctive therapy to diet to slow the progression of atherosclerosis in adult patients as part of a treatment strategy to lower Total-C and LDL-C to target levels.

Primary Prevention of Cardiovascular Disease

In individuals without clinically evident coronary heart disease but with an increased risk of cardiovascular disease based on age > 50 years old in men and > 60 years old in women, hsCRP > 2 mg/L, and the presence of at least one additional cardiovascular disease risk factor such as hypertension, low HDL-C, smoking, or a family history of premature coronary heart disease, Rosuvastatin Calcium is indicated to:

- reduce the risk of stroke
- reduce the risk of myocardial infarction
- reduce the risk of arterial revascularization procedures

Limitations of Use

Rosuvastatin Calcium has not been studied in Fredrickson Type I and V dyslipidemias.

DOSAGE AND ADMINISTRATION:

General Dosing Information

The dose range for Rosuvastatin is 5 to 40 mg orally once daily. The usual starting dose is 10-20 mg.

Rosuvastatin can be administered as a single dose at any time of day, with or without food. The tablet should be swallowed whole.

When initiating Rosuvastatin therapy or switching from another HMG-CoA reductase inhibitor therapy, the appropriate Rosuvastatin starting dose should be utilized first, and only then titrated according to the patient's response and individualized goal of therapy.

After initiation or upon titration of Rosuvastatin, lipid levels should be analyzed within 2 to 4 weeks and the dosage adjusted accordingly.

The 40 mg dose of Rosuvastatin should be used only for those patients who have not achieved their LDL-C goal utilizing the 20 mg dose.

Heterozygous Familial Hypercholesterolemia in Pediatric Patients (10 to 17 years of age)

The usual dose range of Rosuvastatin is 5-20 mg/day; the maximum recommended dose is 20 mg/day (doses greater than 20 mg have not been studied in this patient population). Doses should be individualized according to the recommended goal of therapy. Adjustments should be made at intervals of 4 weeks or more.

Homozygous Familial Hypercholesterolemia

The recommended starting dose of Rosuvastatin is 20 mg once daily. Response to therapy should be estimated from preapheresis LDL-C levels.

Dosing in Asian Patients

In Asian patients, consider initiation of Rosuvastatin therapy with 5 mg once daily due to increased Rosuvastatin plasma concentrations. The increased systemic exposure should be taken into consideration when treating Asian patients not adequately controlled at doses up to 20 mg/day.

Use with Concomitant Therapy

Patients taking cyclosporine

The dose of Rosuvastatin Calcium should not exceed 5 mg once daily.

Patients taking gemfibrozil

Initiate Rosuvastatin Calcium therapy with 5 mg once daily. The dose of Rosuvastatin Calcium should not exceed 10 mg once daily.

Patients taking lopinavir and ritonavir or atazanavir and ritonavir

Initiate Rosuvastatin Calcium therapy with 5 mg once daily. The dose of Rosuvastatin Calcium should not exceed 10 mg once daily.

Dosing in Patients with Severe Renal Impairment

For patients with severe renal impairment (CrCl < 30 mL/min/1.73 m²) not on hemodialysis, dosing of Rosuvastatin Calcium should be started at 5 mg once daily and not exceed 10 mg once daily. Or as prescribed by the physician.

SPECIAL PRECAUTIONS:

Fertility, pregnancy and lactation

Rosuvastatin tablet is contraindicated during pregnancy and lactation. Women of childbearing potential should use appropriate contraceptive measures. Since cholesterol and other products of cholesterol biosynthesis are essential for the development of the fetus, the potential risk from inhibition of HMG-CoA reductase outweighs the advantage of treatment during pregnancy. Animal studies provide limited evidence of reproductive toxicity. If a patient becomes pregnant during use of this product, treatment should be discontinued immediately. Rosuvastatin is excreted in the milk of rats. There are no data with respect to excretion in milk in humans.

Effects on ability to drive and use machines

Studies to determine the effect of Rosuvastatin on the ability to drive and use machines have not been conducted. However, based on its pharmacodynamic properties, Rosuvastatin is unlikely to affect this ability. When driving vehicles or operating machines, it should be taken into account that dizziness may occur during treatment.

PREGNANCY AND LACTATION:

Atherosclerosis is a chronic process and discontinuation of lipid-lowering drugs during pregnancy should have little impact on the outcome of long-term therapy of primary hypercholesterolemia. Cholesterol and other products of cholesterol biosynthesis are essential components for fetal development (including synthesis of steroids and cell membranes). Since HMG-CoA reductase inhibitors decrease cholesterol synthesis and possibly the synthesis of other biologically active substances derived from cholesterol, they may cause fetal harm when administered to pregnant women. Therefore, HMG-CoA reductase inhibitors are contraindicated during pregnancy and in nursing mothers.

Rosuvastatin Calcium SHOULD BE ADMINISTERED TO WOMEN OF CHILDREN BEARING AGE ONLY WHEN SUCH PATIENTS ARE HIGHLY UNLIKELY TO CONCEIVE AND HAVE BEEN INFORMED OF THE POTENTIAL HAZARDS. If the patient become pregnant while taking this drug, therapy should be discontinued immediately and the patient apprised of the potential hazard to the fetus.

CONTRAINDICATIONS:

Rosuvastatin is contraindicated in patients with a known hypersensitivity to any component of the product. Rosuvastatin is contraindicated in patients with active liver disease or with unexplained persistent elevations of serum transaminases.

ADVERSE DRUG REACTIONS:

Rosuvastatin is generally well tolerated. Adverse reactions have usually been mild and transient. In clinical studies of 10,275 patients, 3.7% were discontinued due to adverse experiences attributable to Rosuvastatin. The most frequent adverse events thought to be related to Rosuvastatin were myalgia, constipation, asthenia, abdominal pain, and nausea.

DRUG INTERACTIONS:

Rosuvastatin interacts with alcohol, antacids, birth control pills, cyclosporine, itraconazole; medicines to lower cholesterol or triglycerides (examples: fenofibrate, gemfibrozil, niacin), red yeast rice and Warfarin. Tell your prescriber or health care professional about all other medicines you are taking, including non-prescription medicines, nutritional supplements, or herbal products. Also tell your prescriber or health care professional if you are a frequent user of drinks with caffeine or alcohol, if you smoke, or if you use illegal drugs. These may affect the way your medicine works. Check with your healthcare professional before stopping or starting any of your medicines.

OVERDOSE AND TREATMENT:

There is no specific treatment in the event of overdose. In the event of overdose, the patient should be treated symptomatically and supportive measures instituted as required. Hemodialysis does not significantly enhance clearance of Rosuvastatin.

CAUTION:

Foods, Drugs, Devices, and Cosmetics Act prohibits dispensing without prescription.

For suspected adverse drug reaction, report to the FDA: www.fda.gov/ph. Seek medical attention immediately at the first sign of any adverse drug reaction.

STORAGE CONDITION:

Store at temperatures not exceeding 30°C.

KEEP ALL MEDICINES OUT OF CHILDREN'S REACH.

AVAILABILITY:

Alu/Alu Blister Pack x 10's (Box of 30's)

DRP-6002-01

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Manufactured for
RAINBOW LIFE SCIENCES PVT. LTD.
502, Ambience Court, 5th Floor, Plot No. 2, Sector-19D, Vashi, Navi Mumbai, Thane 400703, India

Manufacturer
ZIM LABORATORIES LTD.
B-21/22 MIDC Area, Kalmeshwar, Nagpur, Maharashtra State, 441501, India