Rosuva®

Rosuvastatin

COMPOSITION

Rosuva® 5 tablet: Each film coated tablet contains Rosuvastatin 5 mg as Rosuvastatin Calcium USP.
Rosuva® 10 tablet: Each film coated tablet contains Rosuvastatin 10 mg as Rosuvastatin Calcium USP.
Rosuva® 20 tablet: Each Each film coated tablet contains Rosuvastatin 20 mg as Rosuvastatin Calcium USP.

PHARMACOLOGY

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. In vivo studies in animals, and in vitro studies in cultured animal and human cells have shown rosuvastatin to have a high uptake into cell and rosuvastatin produces its lipid-modifying effects in two ways. First, it increases the number of hepatic LDL receptors on the cell surface to enhance uptake and catabolism of LDL. Second, rosuvastatin inhibits hepatic synthesis of VLDL, which reduces the total number of VLDL and LDL particles.

Pharmacokinetics

Absorption: Peak plasma concentrations of rosuvastatin were reached 3 to 5 hours following oral dosing. Both peak concentration (Cmax) and area under the plasma concentration-time curve (AUC) increased in approximate proportion to rosuvastatin dose. The absolute bioavailability of rosuvastatin is approximately 20%. Administration of rosuvastatin with food decreased the rate of drug absorption by 20% as assessed by Cmax, but there was no effect on the extent of absorption as assessed by AUC. 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, mostly albumin.
Metabolism: Rosuvastatin is not extensively metabolized; approximately 10% of a radiolabeled 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. Overall, greater than 90% of active plasma HMG-CoA reductase inhibitory activity is accounted for by rosuvastatin.
Elimination: Following oral administration, rosuvastatin and its metabolites are primarily excreted in the feces (90%). The elimination half-life ($t_{1/2}$) of rosuvastatin is approximately 19 hours.

USES AND INDICATIONS

Heterozygous Hypercholesterolemia (Familial and Nonfamilial)
Homozygous Hypercholesterolemia (Familial)
Mixed Dyslipidemia (Fredrickson Type IIa and IIb)

DOSAGE & ADMINISTRATION

Heterozygous Hypercholesterolemia (Familial and Nonfamilial) and Mixed Dyslipidemia (Fredrickson Type IIa and IIb):
The usual recommended starting dose of Rosuvastatin is 10 mg once daily. Initiation of therapy with 5 mg once daily may be considered for patients requiring less aggressive LDL-C reductions or who have predisposing factors for myopathy. For patients with marked hypercholesterolemia (LDL-C > 190 mg/dL) and aggressive lipid targets, a 20-mg starting dose may be considered. The 40-mg dose of Rosuvastatin should be reserved for those patients who have not achieved goal LDL-C at 20 mg. After initiation and/or upon titration of Rosuvastatin, lipid levels should be analyzed within 2 to 4 weeks and dosage adjusted accordingly.
Homozygous Hypercholesterolemia (Familial):
The recommended starting dose of Rosuvastatin is 20 mg once daily in patients with homozygous FH. The maximum recommended daily dose is 40 mg.
Rosuvastatin should be used in these patients as an adjunct to other lipid-lowering treatments (e.g., LDL apheresis) or if such treatments are unavailable.
Dosage in Patients With Renal Insufficiency
No modification of dosage is necessary for patients with mild to moderate renal insufficiency. For patients with severe renal impairment (CLcr<30 mL/min/1.73 m^2) not on hemodialysis, dosing of Rosuvastatin should be started at 5 mg once daily and not to exceed 10 mg once daily.

CONTRAINDICATIONS

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

SIDE EFFECTS

Rosuvastatin is generally well tolerated. The most frequent adverse events thought to be related to rosuvastatin were myalgia, constipation, asthenia, abdominal pain, and nausea.

DRUG INTERACTION

Cytochrome: Rosuvastatin clearance is not dependent on metabolism by cytochrome P450 3A4 to a clinically significant extent. Ketoconazole: Co-administration of ketoconazole with rosuvastatin resulted in no change in plasma concentrations of rosuvastatin. Erythromycin: Co-administration of erythromycin with rosuvastatin decreased AUC and Cmax of rosuvastatin by 20% and 31%, respectively. Itraconazole: Itraconazole resulted in a 39% and 28% increase in AUC of rosuvastatin after 10 mg and 80 mg dosing, respectively. Fluconazole: Co-administration of fluconazole with rosuvastatin resulted in a 14% increase in AUC of rosuvastatin. Warfarin: Co-administration of warfarin (20 mg) with rosuvastatin (40 mg) did not change warfarin plasma concentrations but increased the International Normalized Ratio (INR). Digoxin: Co-administration of digoxin (0.5 mg) with rosuvastatin (40 mg) resulted in no change to digoxin plasma concentrations. Fenofibrate: Co-administration of fenofibrate (67 mg three times daily) with rosuvastatin (10 mg) resulted in no significant changes in plasma concentrations of rosuvastatin or fenofibrate. Gemfibrozil: Co-administration of gemfibrozil (600 mg twice daily for 7 days) with rosuvastatin (80 mg) resulted in a 90% and 120% increase for AUC and Cmax of rosuvastatin, respectively. This increase is considered to be clinically significant. Antacid:
Co-administration of an antacid (aluminum and magnesium hydroxide combination) with rosuvastatin (40 mg) resulted in a decrease in plasma concentrations of rosuvastatin by 54%. Oral contraceptives: Co-administration of oral contraceptives (ethinyl estradiol and norgestrel) with rosuvastatin resulted in an increase in plasma concentrations of ethinyl estradiol and norgestrel by 26% and 34%, respectively.

USE IN PREGNANCY AND LACTATION

Rosuvastatin should be administered to women of childbearing age only when such patients are highly unlikely to conceive and have been informed of the potential hazards. If the patient becomes pregnant while taking this drug, therapy should be discontinued immediately and the patient apprised of the potential hazard to the fetus. It is not known whether rosuvastatin is excreted in human milk.

USE IN PEDIATRIC PATIENTS

The safety and effectiveness in pediatric patients have not been established.

STORAGE

Store below 30°C, in a dry place. Keep all medicines out of reach of children.

HOW SUPPLIED

Rosuva® 5 tablet: Each box contains 1 x 10 / 2 x 10 / 3 x 10 / 5 x 10 / 10 x 10 tablets in Alu-Alu blister pack.
Rosuva® 10 tablet: Each box contains 1 x 10 / 2 x 10 / 3 x 10 / 5 x 10 / 10 x 10 tablets in Alu-Alu blister pack.
Rosuva® 20 tablet: Each box contains 1 x 10 / 2 x 10 / 3 x 10 / 5 x 10 / 10 x 10 tablets in Alu-Alu blister pack.

SQUARE