

Stalip^{Tablet}

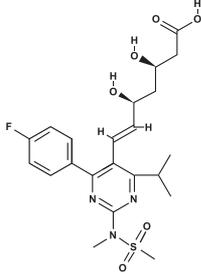
(Rosuvastatin Calcium)

COMPOSITION

STALIP Tablet 5mg	
Each film coated tablet contains:	
Rosuvastatin (as Calcium).....	5mg
(USP specifications)	
STALIP Tablet 10mg	
Each film coated tablet contains:	
Rosuvastatin (as Calcium).....	10mg
(USP specifications)	
STALIP Tablet 20mg	
Each film coated tablet contains:	
Rosuvastatin (as Calcium).....	20mg
(USP specifications)	

DESCRIPTION

STALIP contains rosuvastatin as an active ingredient. Rosuvastatin is in a group of drugs called HMG CoA reductase inhibitors, or "statins." Rosuvastatin reduces levels of "bad" cholesterol (low-density lipoprotein, or LDL) and triglycerides in the blood, while increasing levels of "good" cholesterol (high-density lipoprotein, or HDL). Rosuvastatin is used to lower cholesterol and triglycerides (types of fat) in the blood. It is a synthetic lipid-lowering agent for oral administration. The chemical name for rosuvastatin calcium is bis [(E)-7-[(4-fluorophenyl)-6-isopropyl-2[methyl (methyl sulfonyl) amino] pyrimidin-5-yl] (3R, 5S)-3, 5-dihydroxyhept-6-enoic acid] calcium salt. This compound belongs to the class of organic compounds known as phenyl pyrimidines. These are polycyclic aromatic compounds containing a benzene ring linked to a pyrimidine ring through a CC or CN bond. Pyrimidine is a 6-membered ring consisting of four carbon atoms and two nitrogen centres at the 1- and 3- ring positions.



MECHANISM OF ACTION

Rosuvastatin is a selective and competitive inhibitor of HMG-CoA reductase, the rate-limiting enzyme that converts 3-hydroxy-3-methyl glutaryl 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.

THERAPEUTIC INDICATIONS

STALIP (Rosuvastatin) is indicated for the treatment of:

•Hyperlipidemia and Mixed Dyslipidemia

As adjunctive therapy to diet to reduce elevated Total-C, LDL-C, Apo B, 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 to diet to reduce Total-C, LDL-C and Apo B 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 greater than 190 mg/dL or greater than

160 mg/dL and there is a positive family history of premature cardiovascular disease (CVD) or two or more other CVD risk factors.

•Hypertriglyceridemia

As adjunctive therapy to diet for the treatment of adult patients with hypertriglyceridemia.

•Primary Dys beta lipoproteinemia (Type III Hypolipoproteinemia)

As an adjunct to diet for the treatment of patients with primary dysbetalipoproteinemia (Type III Hyperlipoproteinemia).

•Homozygous Familial Hypercholesterolemia

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 Apo B in adult patients with homozygous familial hypercholesterolemia.

•Slowing of the Progression of Atherosclerosis

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. Prevention of Cardiovascular Events: Prevention of major cardiovascular events in patients who are estimated to have a high risk for a first cardiovascular event, as an adjunct to correction of other risk factors.

DOSAGE AND ADMINISTRATION

General

The dose range for **STALIP** (Rosuvastatin) is 5mg to 40mg orally once daily. The usual starting dose is 10-20mg. **STALIP** (Rosuvastatin) can be administered as a single dose at any time of day, with or without food.

When initiating **STALIP** (Rosuvastatin) therapy or switching from another HMG-CoA reductase inhibitor therapy, the appropriate **STALIP** (Rosuvastatin) starting dose should first be utilized and only then titrated according to the patient's response and individualized goal of therapy. After initiation or upon titration of **STALIP** (Rosuvastatin), lipid levels should be analyzed within 2 to 4 weeks and the dosage adjusted accordingly.

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

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

The usual dose range of **STALIP** (Rosuvastatin) is 5mg/day to 20mg/day, the maximum recommended dose is 20mg/day. 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 **STALIP** (Rosuvastatin) is 20mg once daily. Response to therapy should be estimated from pre-apheresis LDL-C levels.

Elderly

A start dose of 5mg is recommended in patients >70 years. No other dose adjustment is necessary in relation to age.

Dosage in patients with renal insufficiency

The recommended start dose is 5mg in patients with moderate renal insufficiency (creatinine clearance of <60mL/min).

Race

The recommended start dose is 5 mg for patients of Asian ancestry. The dose may be increased at intervals of 4 weeks, if necessary, to a usual maximum of 20mg once daily.

Dosage in patients with pre-disposing factors to myopathy

The recommended start dose is 5mg in patients with predisposing factors to myopathy. The dose may be increased at intervals of 4 weeks. If necessary, to a usual maximum of 20mg once daily.

PHARMACOKINETICS

•Absorption

Maximum plasma concentration is achieved approximately in 5 hours after oral

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(روسوواسٹاٹین کلسیم)

administration. The absolute bioavailability is approximately 20%. Both peak concentration (C_{max}) and area under the plasma concentration-time curve (AUC) increased in approximate proportion to rosuvastatin dose. Administration of rosuvastatin with food did not affect the AUC of rosuvastatin.

•Distribution

Rosuvastatin is taken up extensively by the liver which is the primary site of cholesterol synthesis and LDL-C clearance. The volume of distribution of rosuvastatin is approximately 134 L > Approximately 90% of rosuvastatin is bound to plasma proteins, mainly to albumin. This binding is reversible and independent of plasma concentrations.

•Metabolism

Rosuvastatin undergoes limited metabolism (approximately 10%). The main metabolites identified are the N-desmethyl and lactone metabolites. The N-desmethyl metabolite is approximately 50% less active than rosuvastatin whereas the lactone form is considered clinically inactive. Rosuvastatin accounts for greater than 90% of the circulating HMG-CoA reductase inhibitor activity.

•Excretion

About 90% of an oral dose of rosuvastatin appears in the feces, including absorbed and non-absorbed drugs, and the remainder is excreted in the urine; about 5% of a dose is excreted unchanged in urine. The plasma elimination half-life is approximately 19 hours. The elimination half-life does not increase at higher doses.

SPECIAL POPULATIONS

PRECAUTIONS

Rosuvastatin should be prescribed with caution in patients with predisposing factors for myopathy/rhabdomyolysis. Such factors include:

Renal insufficiency, hypothyroidism, personal or family history of hereditary muscular disorders, previous history of muscular toxicity with another HMG-CoA reductase inhibitor or fibrate, alcohol abuse, age >70 years, situations where an increase in plasma levels may occur, concomitant use of fibrates. In such patients, the risk of treatment should be considered in relation to possible benefit and clinical monitoring is recommended. If creatinine kinase levels are significantly elevated at baseline (>5xULN) treatment should not be started. There is an increase, in serum transaminases [AST (SCOT) or ALT(SGPT)] with HMG-CoA reductase inhibitors, including rosuvastatin.

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. If an increase in ALT or AST of >3 times ULN persist, reduction of dose or withdrawal of rosuvastatin is recommended.

Rosuvastatin should be used with caution in patients who consume substantial quantities of alcohol and/or have a history of chronic liver. A dose reduction should be considered for patients on rosuvastatin therapy with unexplained persistent proletruria and/or hematuria during routine urinalysis testing. There is an increase in HbA1c and fasting serum glucose levels with HMG-CoA reductase inhibitors, including rosuvastatin. Caution should be exercised if rosuvastatin is administered concomitantly with drugs that may decrease the levels or activity of endogenous steroid hormones such as ketoconazole, spironolactone, and cimetidine.

SIDE EFFECTS

Side effects are uncommon. The following side effects should be reported to the prescribing doctor if they persist or get worse: constipation, heartburn, dizziness, insomnia, depression joint pain, cough, memory loss or forgetfulness, confusion, The following rare side effects are more serious. Like all statins, rosuvastatin can possibly cause myopathy, rhabdomyolysis. Stop taking rosuvastatin and contact the prescribing doctor if any of these occur: muscle pain, tenderness, or weakness, lack of energy, fever, chest pain, jaundice: yellowing of the skin or eyes, dark colored, or foamy urine, pain in the upper right part of the abdomen, nausea, extreme tiredness, weakness, unusual bleeding or bruising, loss of appetite, flu-like symptoms, sore throat, chills, or other signs of infection. If any signs of an allergic reaction develop, contact an emergency medical service immediately: rash, hives, itching, difficulty breathing or swallowing, swelling of the face, throat, tongue, lips, eyes, hands, feet, ankles, or lower legs, hoarseness, numbness, or tingling in fingers or toes.

DRUG INTERACTIONS

Coumarin

In patients taking coumarin anticoagulants and rosuvastatin concomitantly, INR should be determined before starting rosuvastatin and frequently enough during early therapy to ensure that no significant alteration of INR occurs.

Gemfibrozil

Gemfibrozil significantly increased rosuvastatin exposure. Therefore, combination therapy with rosuvastatin and gemfibrozil should be avoided. If used, do not exceed rosuvastatin 10mg once daily.

Antacid

The simultaneous dosing of rosuvastatin with an antacid suspension containing aluminum and magnesium hydroxide resulted in a decrease in rosuvastatin plasma concentration of approximately 50%. The antacid should be taken at least 2 hours after rosuvastatin administration.

Niacin

The risk of skeletal muscle effects may be enhanced when rosuvastatin is used in combination with niacin, a reduction in rosuvastatin dosage should be considered.

CONTRAINDICATIONS

Rosuvastatin is contraindicated:

- In patients with hypersensitivity to rosuvastatin or to any of the excipients. In patients with active liver disease including unexplained, persistent elevations of serum transaminases and any serum transaminases elevation exceeding 3x the upper limit of normal (ULN).
- During pregnancy and lactation and in women of childbearing potential not using appropriate contraceptive measures.
- In patients with severe renal insufficiency (Creatinine clearance <30mL/min.)
- In patients with myopathy.
- In patients receiving concomitant cyclosporine.
- In children, younger than 10 years.
- Concomitant use of protease inhibitors in HIV patients.

The 40mg dose is contraindicated in patients with pre-disposing factors for myopathy/rhabdomyolysis. Such factors include:

- Moderate renal insufficiency (Creatinine clearance <60mL/min)
- Hypothyroidism.
- Personal or family history of hereditary muscular disorders.
- Previous history of muscular toxicity with another HMG-CoA reductase inhibitor or fibrate.
- Alcohol abuse.
- Situations where an increase in plasma levels may occur.
- Concomitant use of fibrates
- Asian patients.

OVERDOSAGE

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. Liver function and creatinine kinase levels should be monitored. Hemodialysis is unlikely to be of benefit.

STORAGE

Store between 15-25°C. protect from heat, sunlight & moisture. Keep out of reach of children.

To be sold on prescription of a registered medical practitioner only.

HOW SUPPLIED

STALIP Tablet 5mg
10's, 20's, 30's Tablets

STALIP Tablet 10mg
10's Tablets

STALIP Tablet 20mg
10's Tablets

خوراک و طریقہ استعمال:

ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔

ہدایات:

دوا کو ۱۵-۲۵ ڈگری سینٹی گریڈ درجہ حرارت کے درمیان رکھیں۔

دھوپ، گرمی اور نمی سے بچائیں۔ بچوں کی پہنچ سے دور رکھیں۔

صرف رجسٹرڈ ڈاکٹر کے نسخے کے مطابق فروخت کریں۔

Manufactured by:

PHARMA SOL
PRIVATE LIMITED
Plot # 549, Sundar Industrial Estate,
Lahore, Pakistan.

120mm

171mm