Rosutin®

Rosuvastatin
5 mg, 10 mg and 20 mg Tablet

Description

Rosutin® is a preparation of Rosuvastatin. Rosuvastatin is a member of the drug class of statins, used in combination with exercise, diet, and weight-loss to treat high cholesterol and related conditions, and to prevent cardiovascular disease.

The primary use of rosuvastatin is for the treatment of dyslipidemia. It is recommended to be used only after other measures such as diet, exercise, and weight reduction have not improved cholesterol levels.

Mode 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 (HMG-CoA) to mevalonate, a precursor of sterols, including cholesterol.The primary site of action of rosuvastatin is the liver, the target organ for lowering cholesterol.

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.

Indications

Primary hypercholesterolemia (type IIa including heterozygous familial hypercholesterolemia), mixed dyslipidemia (type IIb), or homozygous familial hypercholesterolemia in patients who have not responded adequately to diet and other appropriate measures; prevention of cardiovascular events in patients at high risk of a first cardiovascular event.

Dosage and Administration

Before treatment initiation the patient should be placed on a standard cholesterol-lowering diet that should continue during treatment. The dose should be individualized according to the goal of therapy and patient response, using current consensus guidelines.

Rosutin® may be given at any time of day, with or without food.

Treatment of hypercholesterolemia

Patient of Asian origin or with risk factors for myopathy or rhabdomyolysis: initially 5 mg once daily increased if necessary to max. 20 mg daily.

Prevention of cardiovascular events:

Patient of Asian origin or with risk factors for myopathy or rhabdomyolysis: initially 5 mg once daily increased if necessary to max. 20 mg daily.

Pediatric Use:

Hyperlipidemia including familial hypercholesterolemia:

Child younger than 6 years: not recommended.

Child 6–9 years: initially 5 mg daily, increased if necessary at intervals of at least 4 weeks to usual max. 10 mg once daily.

Child 10–18 years: initially 5 mg daily, increased if necessary at intervals of at least 4 weeks to usual max. 20 mg once daily.

[Reduced dose required with concomitant atazanavir, darunavir, ezetimibe, fibrate, itraconazole, lopinavir, or tipranavir]

Use in the elderly

Patients > 70 years: A start dose of 5 mg is recommended. No dose adjustment necessary.

Renal insufficiency

Initially 5mg once daily (do not exceed 20mg daily) if eGFR is 30–60 mL/minute/1.73m^2. Avoid if eGFR is less than 30 mL/minute/1.73m^2.

Hepatic impairment

Child-Pugh scores of < 7: no increase in systemic exposure to rosuvastatin.

Child-Pugh scores of 8 and 9: increased systemic exposure has been observed. In these patients an assessment of renal function should be considered.

Child-Pugh scores > 9: no study.

Rosutin® is contraindicated in patients with active liver disease.

Race

Increased systemic exposure has been seen in Asian subjects. The recommended starting dose is 5 mg for patients of Asian ancestry. The 40 mg dose is contraindicated in these patients.

Genetic polymorphisms

Specific types of genetic polymorphisms are known that can lead to increased rosuvastatin exposure. For patients who are known to have such specific types of polymorphisms, a lower daily dose of Rosutin® is recommended.

Dosage in patients with pre-disposing factors to myopathy

The recommended starting dose is 5 mg in patients with predisposing factors to myopathy.

The 40 mg dose is contraindicated in some of these patients.

Contraindications

Rosutin® 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 transaminase elevation exceeding 3 x the upper limit of normal (ULN).
- in patients with severe renal impairment (creatinine clearance < mL/minute/1.73m^2).
- in patients with myopathy.
- in patients receiving concomitant cyclosporine.
- during pregnancy and lactation and in women of childbearing potential not using appropriate contraceptive measures.

Special Warnings and Precautions

Hypothyroidism should be managed adequately before starting treatment with a statin.

Statins should be used with caution in those with a history of liver disease or with a high alcohol intake. There is little information available on a rational approach to liver-function monitoring; however, a NICE guideline1 suggests that liver enzymes should be measured before treatment, and repeated within 3 months and at 12 months of starting treatment, unless indicated at other times by signs or symptoms suggestive of hepatotoxicity. Those with serum transaminases that are raised, but less than 3 times the upper limit of the reference range, should not be routinely excluded from statin therapy. Those with serum transaminases of more than 3 times the upper limit of the reference range should discontinue statin therapy.

Statins should be used with caution in those with risk factors for myopathy or rhabdomyolysis; patients should be advised to report unexplained muscle pain.

Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

Drug Interactions

Cyclosporine

Cyclosporine increased rosuvastatin exposure (AUC) 7-fold. Therefore, in patients taking cyclosporine, the dose of Rosutin® should not exceed 5 mg once daily.

Gemfibrozil

Gemfibrozil significantly increased rosuvastatin exposure. Due to an observed increased risk of myopathy/rhabdomyolysis, combination therapy with Rosutin® and gemfibrozil should be avoided. If used together, the dose of Rosutin® should not exceed 10 mg once daily.

Protease Inhibitors

Coadministration of rosuvastatin with certain protease inhibitors has differing effects on rosuvastatin exposure. Simeprevir, which is a hepatitis C virus (HCV) protease inhibitor, or combinations of atazanavir/ritonavir or lopinavir/ritonavir, which are HIV-1 protease inhibitors, increase rosuvastatin exposure (AUC) up to threefold. For these protease inhibitors, the dose of Rosutin® should not exceed 10 mg once daily. The combinations of fosamprenavir/ritonavir or tipranavir/ritonavir, which are HIV-1 protease inhibitors, produce little or no change in rosuvastatin exposure. Caution should be exercised when rosuvastatin is coadministered with protease inhibitors.

Coumarin Anticoagulants

Rosutin® significantly increased INR in patients receiving coumarin anticoagulants. Therefore, caution should be exercised when coumarin anticoagulants are given in conjunction with Rosutin®. In patients taking coumarin anticoagulants and Rosutin® concomitantly, INR should be determined before starting Rosutin® and frequently enough during early therapy to ensure that no significant alteration of INR occurs.

Niacin

The risk of skeletal muscle effects may be enhanced when Rosutin® is used in combination with lipid-modifying doses (>1 g/day) of niacin; caution should be used when prescribing with Rosutin®.

Fenofibrate

When Rosutin® was coadministered with fenofibrate, no clinically significant increase in the AUC of rosuvastatin or fenofibrate was observed. Because it is known that the risk of myopathy during treatment with statins is increased with concomitant use of fenofibrates, caution should be used when prescribing fenofibrates with Rosutin®.

Colchicine

Cases of myopathy, including rhabdomyolysis, have been reported with statins, including rosuvastatin, coadministered with colchicine, and caution should be exercised when prescribing Rosutin® with colchicine.

Use during Pregnancy and Lactation

Pregnancy Category X: Teratogenic effects.

Rosuvastatin is contraindicated in pregnancy and lactation. Women of child bearing potential should use appropriate contraceptive measures. 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.

Side Effects

Common or very common:

Proteinuria.

Rare:

Hepatitis, jaundice.

Very rare:

Gynecomastia, hematuria, hepatic failure, interstitial lung disease, lupus erythematosus-like reactions, pancreatitis.

Frequency not known:

Alopecia, altered liver function tests, amnesia, arthralgia, asthenia, depression, dizziness, edema, fatigue, gastro-intestinal disturbances, headache, hypersensitivity reactions, hyperglycemia -may be associated with the development of diabetes mellitus (particularly in those already at risk of the condition), myalgia, myopathy, myositis, paresthesia, peripheral neuropathy, pruritus, rash, rhabdomyolysis, sexual dysfunction, sleep disturbance, Stevens-Johnson syndrome, thrombocytopenia, urticaria, visual disturbance.

Muscle effects:

The risk of myopathy, myositis, and rhabdomyolysis associated with statin use is rare. Although myalgia has been reported commonly in patients receiving statins, muscle toxicity truly attributable to statin use is rare. Muscle toxicity can occur with all statins, however the likelihood increases with higher doses.

If muscular symptoms or raised creatine kinase occur during treatment, other possible causes (e.g. rigorous physical activity, hypothyroidism, infection, recent trauma, and drug or alcohol addiction) should be excluded before statin therapy is implicated, particularly if statin treatment has previously been tolerated for more than 3 months. When a statin is suspected to be the cause of myopathy, and creatine kinase concentration is markedly elevated (more than 5 times upper limit of normal), or if muscular symptoms are severe, treatment should be discontinued. If symptoms resolve and creatine kinase concentrations return to normal, the statin should be reintroduced at a lower dose and the patient monitored closely; an alternative statin should be prescribed if unacceptable side-effects are experienced with a particular statin. Statins should not be discontinued in the event of small, asymptomatic elevations of creatine kinase. Routine monitoring of creatine kinase is unnecessary in asymptomatic patients.

Statins should not be discontinued if there is an increase in the blood-glucose concentration or HbA1C as the benefits continue to outweigh the risks.

Interstitial lung disease:

If patients develop symptoms such as dyspnoea, cough, and weight loss, they should seek medical attention.

Overdose

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 CK levels should be monitored. Hemodialysis is unlikely to be of benefit.

Pharmaceutical Precautions

Keep out of the reach of children. Store below 30°C. Keep in the original package in a cool & dry place in order to protect from light and moisture.

Commercial Pack

Rosutin® 5 Tablet: Box containing 30 tablets in 3 x 10's Alu-Alu form packs. Each enteric coated tablet contains Rosuvastatin 5 mg.

Rosutin® 10 Tablet: Box containing 20 tablets in 2 x 10's Alu-Alu form packs. Each enteric coated tablet contains Rosuvastatin 10 mg.

Rosutin® 20 Tablet: Box containing 30 tablets in 3 x 10's Alu-Alu form packs. Each enteric coated tablet contains Rosuvastatin 20 mg.

BEXIMCO PHARMA

Manufactured by
BEXIMCO PHARMACEUTICALS LTD.
TONGI, BANGLADESH