ROSULIP

Rosuvastatin 5/10/20

GENERIC NAME: Rosuvastatin.

THERAPEUTIC CATEGORY: Antihyperlipidemic.

PHARMACOLOGIC CLASS: HMG-COA Reductase Inhibitor.

COMPOSITION AND PRESENTATION:

Rosulip 5:

Compostion:
Film coated tablet Rosuvastin calcium equivalent to 5 mg Rosuvastatin IP
Presentation:
30 tablets X 5 blisters

Rosulip 10:

Composition:
Film coated tablet Rosuvastin calcium equivalent to 10 mg Rosuvastatin IP
Presentation:
30 tablets X 5 blisters

Rosulip 20

Composition:
Film coated tablet Rosuvastin calcium equivalent to 20 mg Rosuvastatin IP
Presentation:
20 tablets X 5 blisters

Mechanism of Action:

Rosuvastatin is a synthetic statin that acts as a reversible competitive inhibitor of 3-hydroxy-3-methylglutaryl-CoA (HMG-CoA) reductase. HMG-CoA reductase is the most important rate limiting enzyme that converts HMG-CoA to mevalonate, a precursor for cholesterol synthesis. Rosuvastatin is relatively selective for liver, the target organ for cholesterol lowering. Rosuvastin also 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 molecules.

Indication:

Atherosclerosis.
High Cholesterol.
Homozygous familial hypercholesterolemia.
Heterozygous familial hypercholesterolemia.
Hyperlipoproteinemia.

Hyperlipoproteinemia Type IIa, Elevated LDL.
Hyperlipoproteinemia Type IIb, Elevated LDL VLDL.
Hyperlipoproteinemia Type III, Elevated beta –VLDL IDL.
Hyperlipoproteinemia Type IV, Elevated VLDL.
Prevention of cardiovascular disease.

Dosage:

- The recommended starting dose is 10 mg with titration to 20 mg only if necessary. Caution is advices when increasing the dose to 40 mg.
- Safety and efficacy of doses greater than 20 mg have not been studied in children and adolescents.
- Rosuvastatin is not recommended to use in the children under 10 years old.
- A start dose of 5 mg is recommended in patients >70 years .No other dose adjustment is necessary in relation to age.
- No dose adjustment is necessary in patients with mild to moderate renal impairment. The 40 mg dose is contraindicated in patients with moderate renal impairment.
- The recommended start dose is 5 mg for patients of Asian ancestry. The 40 mg dose is contraindicated in these patients because pharmacokinetic studies show an increase in exposure in Asian subjects compared with Caucasians

Pharmacokinetic profile:

- Maximum plasma concentration is achieved approximately 5 hours after oral administration.
- Rosuvastatin is taken up by liver extensively.
- Approximately 90 % of Rosuvastatin is bound to plasma proteins, mainly to albumin.
- Approximately 10 % of the drug undergo metabolism. The main metabolites identified are the N-desmethyl (50 % less active than parent compound) and lactone metabolites (clinically inactive).
- Approximately 90% of the rosuvastatin dose is excreted unchanged in the faeces (consisting of absorbed and non-absorbed active substance) and the remaining part is excreted in urine. Approximately 5% is excreted unchanged in urine.
- The plasma elimination half-life is approximately 19 hours (The elimination half-life does not increase at higher doses).
- As with other HMG-CoA reductase inhibitors, the hepatic uptake of Rosuvastatin involves the membrane transporter OATP-C. This transporter is important in the hepatic elimination of Rosuvastatin.

Adverse Effect:

Adverse effects are generally mild and transient. As with other HMG-CoA reductase inhibitors, the incidence of adverse drug reactions tends to be dose dependent. Some adverse effect seen with this drug is as follow.

- Myalgia, asthenia, diabetes mellitus, headache, dizziness, constipation, nausea, abdominal pains are common side effect of Rosuvastatin.

- Hypersensitivity reactions including angioedema, pruritus, rash and urticaria, pancreatitis, myopathy (including myositis) and rhabdomyolysis are rarely seen side effect of Rosuvastatin.

Special Precaution:

- Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.
- Should not be used in any patient with an acute or serious condition suggestive of myopathy or predisposing to the development of renal failure secondary to rhabdomyolysis (e.g. sepsis, hypotension, major surgery, trauma, severe metabolic, endocrine and electrolyte disorders; or uncontrolled seizures).
- Should be used with caution in patients who consume excessive quantities of alcohol and/or have a history of liver disease. It is recommended that liver function tests be carried out prior to, and 3 months following, the initiation of treatment. Rosuvastatin should be discontinued or the dose reduced if the level of serum transaminases is greater than 3 times the upper limit of normal.
- In patients with secondary hypercholesterolemia caused by hypothyroidism or nephrotic syndrome, the underlying disease should be treated prior to initiating therapy with Rosuvastin.

.

Contraindications.

- Hypersensitive to Rosuvastatin or to any of the excipient.
- Liver disease.
- Severe renal impairment.
- Myopathy.
- Patient receiving concomitant cyclosporine.
- Pregnancy and lactation.
- 40 mg dose is contraindicated in the patient with pre disposing factor for myopathy / rhabdomyolysis, pediatrics.

Interaction with other drugs

- Vitamin K antagonists
- Very rare cases of rhabdomyolysis have been reported with the use of Ezetimibe in combination with HMG-CoA reductase inhibitors. A pharmacodynamic interaction cannot be excluded and caution should be exercised with their combined use.
- Concomitant use of Rosuvastatin and Gemfibrozil resulted in a 2-fold increase in Rosuvastatin C_{max} and AUC.
- Gemfibrozil, fenofibrate, other fibrates and lipid lowering doses (> or equal to 1g/day) of niacin (nicotinic acid) increase the risk of myopathy when given concomitantly with

HMG-CoA reductase inhibitors, probably because they can produce myopathy when given alone. The 40 mg dose is contraindicated with concomitant use of a fibrate.

- Although the exact mechanism of interaction is unknown, concomitant protease inhibitor use may strongly increase Rosuvastatin exposure.
- The simultaneous dosing of Rosuvastatin with an antacid suspension containing Aluminium and Magnesium hydroxide resulted in a decrease in Rosuvastatin plasma concentration of approximately 50%. This effect was mitigated when the antacid was dosed 2 hours after Rosuvastatin.
- Concomitant use of Rosuvastatin and Erythromycin resulted in a 20% decrease in AUC (0-t) and a 30% decrease in C_{max} of Rosuvastatin. This interaction may be caused by the increase in gut motility caused by erythromycin.
- Concomitant use of Rosuvastatin and an oral contraceptive resulted in an increase in Ethinyl Estradiol and Norgestrel AUC of 26% and 34%, respectively. These increased plasma levels should be considered when selecting oral contraceptive doses.

For further information, please contact:
Market Planning Department
Deurali-Janta Pharmaceuticals Pvt. Ltd.
GPO Box 4239, 355 Hattisar Road, Kamalpokhari, Kathmandu, Nepal.
Tel: 4435167/68/69 E-mail: mplanning@deuralijanta.com Website: www.deuralijanta.com