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For the use only of a Registered Medical Practitioner or a Hospital or a Laboratory only.

ROSUCOR TABLETS 10 MG

(Rosuvastatin Calcium Tablets 10mg)

NAME AND STRENGTH OF ACTIVE SUBSTANCE (S)

Rosuvastatin Calcium Tablets 10mg

Each film coated tablet contains

Rosuvastatin Calcium 10.400 equivalent to Rosuvastatin 10 mg

DOSAGE FORM

Film coated Tablets

PRODUCT DESCRIPTION

ROSUCOR TABLETS 10 MG: White to off white colored, round, biconvex, film coated tablets with break line on one side and plain on other side

CLINICAL PHARMACOLOGY

Pharmacodynamics:

Rosuvastatin is a 3-hydroxy-3-methyl glutaryl coenzyme A (HMG-CoA) reductase inhibitor indicated for the treatment of hyperlipidemia. Rosuvastatin is a selective and competitive inhibitor of HMG-CoA reductase. HMG-CoA reductase is a 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. It differs structurally from other statins, containing a polar methane sulphonamide group which confers relative hydrophilicity. The relative hydrophilicity of rosuvastatin imparts greater selectivity for uptake into hepatic versus nonhepatic cells. 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. In preclinical studies, the potency of rosuvastatin has been found to be greater than that of other statins (i.e. atorvastatin, simvastatin, pravastatin, lovastatin, cerivastatin, and fluvastatin). Rosuvastatin reduces elevated LDL-cholesterol, total cholesterol and triglycerides and increases HDL-cholesterol. It also lowers ApoB, nonHDL-C, VLDL-C, VLDL-TG and increases ApoA-I. It also lowers the LDL-C/ HDL-C, total C/HDL-C and non HDL-C/HDL-C and the ApoB/ApoA-I ratios.

Pharmacokinetics:

Absorption: Oral rosuvastatin appears to be well absorbed. Maximum rosuvastatin plasma concentrations are achieved approximately 3-5 hours after oral administration. Peak plasma levels and AUC values are approximately linear over the dose range of 5-80 mg.

Distribution: Rosuvastatin is taken up extensively by hepatic versus non hepatic tissue attributed to its relative hydrophilicity. The volume of distribution of rosuvastatin is approximately 134 L.

Metabolism: Rosuvastatin undergoes limited metabolism (about 10%), primarily via cytochrome P 450 isoenzymes 2C9 and 2C19; there is essentially no metabolism by cytochrome P 450-3A4, indicating a low propensity for drug interactions compared to other statins. It is mainly metabolized to the N-desmethyl metabolite and the lactone metabolite. The N-desmethyl metabolite is the active metabolite. Rosuvastatin accounts for greater than 90% of the circulating HMG-CoA reductase inhibitor activity.

Excretion: Approximately 90% of rosuvastatin is excreted as unchanged drug in the faeces and the remaining part is excreted in urine. The plasma elimination half-life is 13-20 hours. The elimination half-life is not dose dependent.

Special populations:

Age and sex: There was no clinically relevant effect of age or sex on the pharmacokinetics of rosuvastatin.

Renal insufficiency: The pharmacokinetics is not affected by mild to moderate renal impairment.

Hepatic insufficiency: The pharmacokinetics is not affected by mild to moderate hepatic impairment.

Race: Pharmacokinetic studies reported an increase in exposure in Asian subjects compared with Caucasians.

INDICATIONS:

1. Mixed dyslipidaemia (type IIb) as an adjunct to diet when response to diet and exercise is inadequate.
2. Homozygous familial hypercholesterolaemia, either alone or as an adjunct to diet and other lipid lowering treatments (e.g. LDL apheresis) when response to diet and exercise is inadequate.

CONTRAINDICATIONS:

Rosucor 10 is contraindicated in patients receiving concomitant cyclosporine.

- Prior hypersensitivity to Rosuvastatin
- Pregnant and lactating females
- Patients with active liver disease including unexplained, persistent elevations of serum transaminases and any serum transaminase elevation exceeding 3x the upper limit of normal (ULN).
- Patients with severe renal impairment (Creatine clearance <30ml/min)
- Patients with myopathy

WARNINGS AND PRECAUTIONS:

Skeletal Muscle Effects

Gemfibrozil increases the risk of myopathy when given concomitantly with some HMG-CoA reductase inhibitors. Therefore, the combination of rosuvastation and gemfibrozil is not recommended. The benefit of further alterations in lipid levels by the combined use of rosuvastatin with fibrates or niacin should be carefully weighed against the potential risks of such combinations.

General:

Rosuvastatin should be used with precaution in:

- Patients with history of hypersensitivity to other statins.
- Patients who consume excessive quantities of alcohol, 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. It is recommended that liver function tests be carried out prior to, and 3 months following, the initiation of treatment with rosuvastatin.
- Patients with myopathy. Uncomplicated myalgia and myopathy have been reported in rosuvastatin treated patients. Patients should be asked to report inexplicable muscle pain or weakness immediately, particularly if associated with malaise or fever. Creatine Kinase (CK) levels should be measured in these patients. Rosuvastatin therapy should be discontinued if CK levels are markedly elevated (>10xULN) or, if on clinical grounds, myopathy is diagnosed or suspected.
- The risk of myopathy during treatment with rosuvastatin may be increased with concurrent administration of other lipid-lowering therapies or cyclosporine. The benefit of further alterations in lipid levels by the combined use of rosuvastatin with fibrates or niacin should be carefully weighed against the potential risks of this combination. Combination therapy with rosuvastatin and gemfibrozil should generally be avoided.
- Patient with an acute, 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).
- Rosuvastatin is not expected to affect the ability to drive or use machines.

Myasthenia gravis/Ocular Myasthenia

In few cases, statins have been reported to induce de novo or aggravate pre-existing myasthenia gravis or ocular myasthenia. Rosucor 10 should be discontinued in case of aggravation of symptoms. Recurrences when the same or a different statin was (re-) administered have been reported.

Renal effects: Proteinuria, detected by dipstick testing and mostly tubular in origin, has been observed in patients treated with higher doses of rosuvastatin, in particular 40 mg. where it was transient or intermittent in most cases. Proteinuria has not been shown to be predictive of acute or progressive renal disease. An assessment of renal function should be considered during routine follow-up of patients treated with a dose of 40 mg.

Liver: 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.

There have been very rare reports of an immune-mediated necrotizing myopathy (IMNM) during or after treatment with some statins. IMNM is clinically characterized by:

- persistent proximal muscle weakness and elevated serum creatine kinase, which persist despite discontinuation of statin treatment;
- muscle biopsy showing necrotizing myopathy without significant inflammation;
- improvement with immunosuppressive agents.

CARCINOGENESIS, MUTAGENESIS, IMPAIRMENT OF FERTILITY:

Preclinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity and carcinogenicity potential. In a rat pre and postnatal study, reproductive toxicity was evident from reduced litter sizes, litter weight and pup survival. These effects were observed at maternally toxic doses at systemic exposures several times above the therapeutic exposure level.

PREGNANCY: TERATOGENIC EFFECTS:

Rosuvastatin should not be used during pregnancy as the safety of rosuvastatin during pregnancy has not been established. Women of childbearing potential should use adequate birth-control measures when rosuvastatin is used. The possibility that a woman of childbearing potential is pregnant at the time of institution of therapy should be considered. A negative result for pregnancy test having sensitivity down to at least 50 mIU/mLfor hCG should be obtained prior to rosuvastatin therapy. Since cholesterol and other products of cholesterol biosynthesis are essential for the development of the foetus, the potential risk from inhibition of HMG-CoA reductase outweighs the advantage of treatment during pregnancy. If a patient becomes pregnant during use of this product, treatment should be discontinued immediately.

NURSING MOTHERS:

Rosuvastatin should not be used during lactation as the safety of rosuvastatin during lactation has not been established. Rosuvastatin is excreted in the milk of rats. There are no data with respect to excretion in milk in humans.

PEDIATRIC USE:

Pediatric experience is limited to a small number of children (aged 8 years or above) with homozygous familial hypercholesterolaemia. Use in children should be supervised by specialists.

INTERACTIONS WITH OTHER MEDICAMENTS:

Effect of co-administered medicinal products on rosuvastatin

Transporter protein inhibitors: Rosuvastatin is a substrate for certain transporter proteins including the hepatic uptake transporter OATP1B1 and efflux transporter BCRP. Concomitant administration of Rosuvastatin with medicinal products that are inhibitors of these transporter proteins may result in increased rosuvastatin plasma concentrations and an increased risk of myopathy.

Ciclosporin: During concomitant treatment with Rosuvastatin and ciclosporin, rosuvastatin AUC values were on average 7 times higher. Rosuvastatin is contraindicated in patients receiving concomitant ciclosporin. Concomitant administration did not affect plasma concentrations of ciclosporin.

Protease inhibitors: Although the exact mechanism of interaction is unknown, concomitant protease inhibitor use may strongly increase rosuvastatin exposure. Co-administration of 10 mg rosuvastatin and a combination product of two protease inhibitors (300 mg atazanavir / 100 mg ritonavir) were associated with an approximately three-fold and seven-fold increase in rosuvastatin AUC and C_{max} respectively. The concomitant use of Rosuvastatin and some protease inhibitor combinations may be considered after careful consideration of Rosuvastatin dose adjustments based on the expected increase in rosuvastatin exposure.

Gemfibrozil and other lipid-lowering products: 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. These patients should also start with the 5 mg dose.

Ezetimibe: Concomitant use of 10 mg Rosuvastatin and 10 mg ezetimibe resulted in a 1.2 fold increase in AUC of rosuvastatin in hypercholesterolaemic subjects. A pharmacodynamic interaction, in terms of adverse effects, between Rosuvastatin and ezetimibe cannot be ruled out.

Antacid: 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. The clinical relevance of this interaction has not been reported.

Erythromycin: Concomitant use of Rosuvastatin and erythromycin resulted in a 20% decrease in AUC and a 30% decrease in C_{max} of rosuvastatin. This interaction may be caused by the increase in gut motility caused by erythromycin.

Cytochrome P450 enzymes: Results from *in vitro* and in vivo studies reported that rosuvastatin is neither an inhibitor nor an inducer of cytochrome P450 isoenzymes. In addition, rosuvastatin is a poor substrate for these isoenzymes. Therefore, drug interactions resulting from cytochrome P450-mediated metabolism are not expected. No clinically relevant interactions have been reported between rosuvastatin and either fluconazole (an inhibitor of CYP2C9 and CYP3A4) or ketoconazole (an inhibitor of CYP2A6 and CYP3A4).

Interactions requiring rosuvastatin dose adjustments: When it is necessary to co-administer Rosuvastatin with other medicinal products known to increase exposure to rosuvastatin, doses of Rosuvastatin should be adjusted. Start with a 5 mg once daily dose of Rosuvastatin if the expected increase in exposure (AUC) is approximately 2-fold or higher. The maximum daily dose of Rosuvastatin should be adjusted so that the expected rosuvastatin exposure would not likely exceed that of a 40 mg daily dose of Rosuvastatin taken without interacting medicinal products, for example a 20 mg dose of Rosuvastatin with gemfibrozil (1.9-fold increase), and a 10 mg dose of Rosuvastatin with combination ritonavir/atazanavir (3.1-fold increase).

Effect of rosuvastatin on co-administered medicinal products

Vitamin K antagonists: As with other HMG-CoA reductase inhibitors, the initiation of treatment or dosage up-titration of Rosuvastatin in patients treated concomitantly with vitamin K antagonists (e.g. warfarin or another coumarin anticoagulant) may result in an increase in International Normalised Ratio (INR). Discontinuation or down-titration of Rosuvastatin may result in a decrease in INR. In such situations, appropriate monitoring of INR is desirable.

Oral contraceptive/hormone replacement therapy (HRT): 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. There are no pharmacokinetic data available in subjects taking concomitant Rosuvastatin and HRT and therefore a similar effect cannot be excluded.

Other medicinal products:

Fusidic Acid: As with other statins, muscle related events, including rhabdomyolysis, have been reported in post-marketing experience with rosuvastatin and fusidic acid given concurrently.

Therefore, the combination rosuvastatin and fusidic acid is not recommended. If possible, temporary suspension of rosuvastatin treatment is recommended. If unavoidable, patients should be closely monitored.

Paediatric population: Interaction studies have only been reported in adults. The extent of interactions in the paediatric population is not known. Concurrent use of fibrates may cause severe myositis and myoglobinuria.

ADVERSE EFFECTS/UNDESIRABLE EFFECTS:

The adverse events seen with Rosuvastatin are generally mild and transient.

Immune system disorders

Hypersensitivity reactions including angioedema

Nervous system disorders

Headache, dizziness

Frequency 'not known': myasthenia gravis

Eye disorders

Frequency 'not known': ocular myasthenia

Gastrointestinal disorders

Constipation, nausea, abdominal pain, pancreatitis

Skin and subcutaneous tissue disorders

Pruritus, rash and urticaria

Musculoskeletal, connective tissue and bone disorders

Myalgia, myopathy (including myositis) and rhabdomyolysis

Musculoskeletal disorders

Frequency not known: Immune-mediated necrotizing myopathy

General disorders

Asthenia

As with other HMG-CoA reductase inhibitors, the incidence of adverse drug reactions tends to be dose dependent.

Renal Effects: Proteinuria, detected by dipstick testing and mostly tubular in origin, has been observed in patients treated with Rosuvastatin. Shifts in urine protein from none or trace to ++ or more were seen in patients at some time during treatment with 10 mg, 20 mg and 40 mg. A minor increase in shift from none or trace to + was observed with the 20 mg dose. In most cases, proteinuria decreases or disappears spontaneously on continued therapy.

Haematuria has been observed in patients treated with Rosuvastatin.

Skeletal muscle effects: Effects on skeletal muscle e.g. myalgia, myopathy (including myositis) and, rhabdomyolysis with and without acute renal failure have been reported in Rosuvastatin-treated patients with all doses and in particular with doses > 20 mg.

A dose-related increase in CK levels has been observed in patients taking Rosuvastatin. If CK levels are elevated (>5xULN), treatment should be discontinued.

Liver Effects: As with other HMG-CoA reductase inhibitors, a dose-related increase in transaminases has been observed.

In addition to the above, the following adverse events have also been reported with Rosuvastatin:

Gastrointestinal disorders: diarrhoea.

Hepatobiliary disorders: jaundice, hepatitis, increased transaminases.

Musculoskeletal disorders: arthralgia.

Nervous system disorders: Polyneuropathy, memory loss.

Renal disorders: Haematuria.

Skin and subcutaneous tissue disorders: Stevens-Johnson syndrome.

The reporting rates for rhabdomyolysis, serious renal events and serious hepatic events (consisting mainly of increased hepatic transaminases) are higher at the 40 mg dose.

There have been rare post-marketing reports of cognitive impairment (e.g. memory loss, forgetfulness, amnesia, memory impairment, confusion) associated with statin use. These cognitive issues have been reported for all statins. The reports are generally non-serious and reversible upon statin discontinuation, with variable times to symptom onset (1 day to years) and symptom resolution (median 3 weeks).

Increase in HbA1c and fasting blood glucose have been reported with statins. The risk of hyperglycemia, however, is outweighed by the reduction in vascular risk with statins.

OVERDOSAGE 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. Liver function and CK levels should be monitored. Haemodialysis is unlikely to be of benefit.

RECOMMENDED DOSAGE:

Adult dose:

The usual start dose is Rosucor 5-10 mg once daily and the majority of patients are controlled at this dose. A dose adjustment to 20 mg can be made after 4 weeks, if necessary. Rosuvastatin 40 mg should only be used in patients with severe hypercholesterolaemia (including those with familial hypercholesterolaemia) who do not achieve their treatment goal on 20 mg. Rosucor may be given at any time of day, with or without food. The patient should be placed on a standard cholesterol-lowering diet that should continue during treatment.

Dosage on Asian Patients

Initiation of rosucor therapy with 5 mg once daily should be considered for Asian patients. The potential for Increased systemic exposures relative to Caucasians is relevant when considering escalation of dose in cases where hypercholesterolaemia is not adequately controlled at doses of 5 , 10 or 20 mg once daily.

Pediatric Use:

The safety and effectiveness in children have not been established. Pediatric experience is limited to a small number of children (aged 8 years or above) with homozygous familial hypercholesterolaemia. Use in children should be supervised by specialists.

Geriatric Use: No dose adjustment required.

Dosage in patients with renal insufficiency:

No dose adjustment is necessary in patients with mild to moderate renal impairment.

The use of ROSUCOR in patients with severe renal impairment is contraindicated.

Dosage in patients with hepatic impairment:

Increased systemic exposure has been observed in subjects with Child-Pugh scores of 8 and 9. In these patients an assessment of renal function should be considered. There is no experience in subjects with Child-Pugh scores above 9. ROSUCOR is contraindicated in patients with active liver disease.

Dosage in patients with pre-disposing factors to myopathy

The recommended start dose is 5 mg in patients with pre-disposing factors to myopathy.

Concomitant Therapy:

Rosuvastatin is a substrate of various transporter proteins (e.g. OATP1B1 and BCRP). The risk of myopathy (including rhabdomyolysis) is increased when rosuvastatin is administered concomitantly with certain medicinal products that may increase the plasma concentration of rosuvastatin due to interactions with these transporter proteins (e.g. certain protease inhibitors including combinations of ritonavir with atazanavir, lopinavir, and /or tipranavir). Whenever possible, alternatively medications should be considered, and if necessary, consider temporarily discontinuining Rosucor 10 therapy. In situations where co-adminstration of these medicinal products with rosuvastatin is unavoidable, the benefit and risk of concurrent treatment and rosuvastatin dosing adjustments should be carefully considered.

Mode of Administration: Oral

STORAGE CONDITIONS:

Store below 30^{O}C, Protect from moisture and light.

Keep out of reach of children.

PACKAGING AVAILABLE:

Rosucor Tablets are available in Alu-Alu blister strip of 1 x 10, 3 x 10, & 10 x 10 tablets Not all presentations or all pack size may be marketed.

DATE OF REVISION OF PACKAGE INSERT:

17th June, 2025

torrent PHARMA

Manufactured by :

TORRENT PHARMACEUTICALS LTD.

Indrad-382 721, Dist. Mehsana, INDIA.

PRODUCT NAME	:	Rosucor 10 mg	**COUNTRY :** Malaysia	**LOCATION :** Chhatral		**Supersedes A/W No.:**	
ITEM / PACK	:	Insert	**NO. OF COLORS:** 1	**REMARK :**			
DESIGN STYLE	:	Front/Back	**PANTONE SHADE NOS.:**	**SUBSTRATE :**			
CODE	:	xxxxxxxxx-5253	Black	**Activities**	**Department**	**Name**	**Signature**	**Date**
DIMENSIONS (MM)	:	180 x 280		Prepared By	**Pkg.Dev**			
ART WORK SIZE	:	S/S		Reviewed By	**Pkg.Dev**			
DATE	:	17-06-2025		Approved By	**Quality**			

This colour proof is not colour binding. Follow Pantone shade reference for actual colour matching.