RAPIVAST 20
Rosuvastatin Tablets BP 20mg

COMPOSITION:
Each Film Coated Tablet Contains:
Rosuvastatin Calcium BP
Eq. to Rosuvastatin 20 mg
Excipients q.s.
Colour: Quinoline Yellow

DESCRIPTION
RAPIVAST 20 contains Rosuvastatin belongs to the class of medicines known as statins, which reduces bad cholesterol (low-density lipoprotein-LDL) and glyceride level, thereby reducing the risk of heart attack and stroke in the future.

PHARMACODYNAMICS
Pharmacotherapeutic group: HMG-CoA reductase inhibitors
ATC code: C10AA07
Mechanism 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 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.

PHARMACOKINETICS
Absorption
Maximum rosuvastatin plasma concentrations are achieved approximately 5 hours after oral administration. The absolute bioavailability is approximately 20%.
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.
Biotransformation
Rosuvastatin undergoes limited metabolism (approximately 10%). In vitro metabolism studies using human hepatocytes indicate that rosuvastatin is a poor substrate for cytochrome P450-based metabolism. CYP2C9 was the principal isoenzyme involved, with 2C19, 3A4 and 2D6 involved to a lesser extent. 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.
Elimination
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. The geometric mean plasma clearance is approximately 50 litres/hour (coefficient of variation 21.7%). 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.

THERAPEUTIC INDICATIONS
Treatment of hypercholesterolaemia
Adults, adolescents and children aged 6 years or older with primary hypercholesterolaemia (type IIa including heterozygous familial hypercholesterolaemia) or mixed dyslipidaemia (type IIb) as an adjunct to diet when response to diet and other non-pharmacological treatments (e.g. exercise, weight reduction) is inadequate.
Adults, adolescents and children aged 6 years or older with homozygous familial hypercholesterolaemia as an adjunct to diet and other lipid lowering treatments (e.g. LDL apheresis) or if such treatments are not appropriate.
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.

POSOLOGY AND METHOD OF ADMINISTRATION
Posology
Before treatment initiation the patient should be placed on a standard cholesterol-lowering diet that should continue during treatment. The dose should be individualised according to the goal of therapy and patient response, using current consensus guidelines.
Rosuvastatin may be given at any time of day, with or without food.
Treatment of hypercholesterolaemia
The recommended start dose is 5 or 10 mg orally once daily in both statin-naïve or patients switched from another HMG CoA reductase inhibitor. The choice of start dose should take into account the individual patient's cholesterol level and future cardiovascular risk as well as the potential risk for adverse reactions. A dose adjustment to the next dose level can be made after 4 weeks. In light of the increased reporting rate of adverse reactions with the 40 mg dose compared to lower doses, a final titration to the maximum dose of 40 mg should only be considered in patients with severe hypercholesterolaemia at high cardiovascular risk (in particular those with familial hypercholesterolaemia), who do not achieve their treatment goal on 20 mg, and in whom routine follow-up will be performed. Specialist supervision is recommended when the 40 mg dose is initiated.
Prevention of cardiovascular events
In the cardiovascular events risk reduction study, the dose used was 20 mg daily.
Paediatric population
Paediatric use should only be carried out by specialists.
Children and adolescents 6 to 17 years of age (Tanner Stage II-V)
Heterozygous familial hypercholesterolaemia
In children and adolescents with heterozygous familial hypercholesterolaemia the usual start dose is 5 mg daily.
- In children 6 to 9 years of age with heterozygous familial hypercholesterolaemia, the usual dose range is 5-10 mg orally once daily. Safety and efficacy of doses greater than 10 mg have not been studied in this population.
- In children 10 to 17 years of age with heterozygous familial hypercholesterolaemia, the usual dose range is 5-20 mg orally once daily. Safety and efficacy of doses greater than 20 mg have not been studied in this population.

Titration should be conducted according to the individual response and tolerability in paediatric patients, as recommended by the paediatric treatment recommendations. Children and adolescents should be placed on standard cholesterol-lowering diet before rosuvastatin treatment initiation; this diet should be continued during rosuvastatin treatment.
Homozygous familial hypercholesterolaemia
In children 6 to 17 years of age with homozygous familial hypercholesterolaemia, the recommended maximum dose is 20 mg once daily. A starting dose of 5 to 10 mg once daily depending on age, weight and prior statin use is advised. Titration to the maximum dose of 20 mg once daily should be conducted according to the individual response and tolerability in paediatric patients, as recommended by the paediatric treatment recommendations. Children and adolescents should be placed on standard cholesterol-lowering diet before rosuvastatin treatment initiation; this diet should be continued during rosuvastatin treatment. There is limited experience with doses other than 20 mg in this population.
The 40 mg tablet is not suitable for use in paediatric patients.
Children younger than 6 years
The safety and efficacy of use in children younger than 6 years has not been studied. Therefore, Rosuvastatin is not recommended for use in children younger than 6 years.
Use in the elderly
A start dose of 5 mg is recommended in patients >70 years. No other dose adjustment is necessary in relation to age.
Dosage in patients with renal insufficiency
No dose adjustment is necessary in patients with mild to moderate renal impairment. The recommended start dose is 5 mg in patients with moderate renal impairment (creatinine clearance <60 ml/min). The 40 mg dose is contraindicated in patients with moderate renal impairment. The use of rosuvastatin in patients with severe renal impairment is contraindicated for all doses.
Dosage in patients with hepatic impairment
There was no increase in systemic exposure to rosuvastatin in subjects with Child-Pugh scores of 7 or below. However, 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. Rosuvastatin is contraindicated in patients with active liver disease.
Race
Increased systemic exposure has been seen in Asian subjects. The recommended start dose is 5 mg for patients of Asian ancestry.
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 rosuvastatin is recommended.
Dosage in patients with pre-disposing factors to myopathy
The recommended start dose is 5 mg in patients with predisposing 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. ciclosporin and certain protease inhibitors including combinations of ritonavir with atazanavir, lopinavir, and/or tipranavir). Whenever possible, alternative medications should be considered, and, if necessary, consider temporarily discontinuing rosuvastatin therapy. In situations where coadministration of these medicinal products with rosuvastatin is unavoidable, the benefit and the risk of concurrent treatment and rosuvastatin dosing adjustments should be carefully considered.

CONTRAINDICATION
Rosuvastatin is contraindicated:
- In patients with hypersensitivity to the active substance 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 times the upper limit of normal (ULN).
- In patients with severe renal impairment (creatinine clearance <30 ml/min).
- In patients with myopathy.
- In patients receiving concomitant combination of sofosbuvir/velpatasvir/voxilaprevir.
- In patients receiving concomitant ciclosporin.
- During pregnancy and lactation and in women of childbearing potential not using appropriate contraceptive measures. The 40 mg dose is contraindicated in patients with pre-disposing factors for myopathy/ rhabdomyolysis. Such factors include:
- Moderate renal impairment (creatinine clearance < 60 ml/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
- Asian patients
- Concomitant use of fibrates.

SPECIAL WARNING AND PRECAUTION FOR USE
A prolonged intake of ROSUVASTATIN may cause muscular disorders like myopathy and rhabdomyolysis with kidney damage. A person taking excess alcohol and affected with liver disease should consult a doctor before its intake. Caution should be exercised if you are taking any blood thinner or anticoagulants like warfarin or coumarin. At least 2 hours gap should be maintained between intake of ROSUVASTATIN and antacids like magnesium hydroxide and aluminium hydroxide. Increases in HbA1c and fasting glucose levels can be observed if a person regularly takes ROSUVASTATIN. So you should tell the doctor before having these diabetes tests. Patients with proteinuria (protein in urine) or haematuria (blood in urine) should tell the doctor before taking the ROSUVASTATIN, as it might require dose adjustment. It is recommended that you should have a liver enzyme test regularly if you are regularly taking ROSUVASTATIN.

INTERACTION WITH OTHER MEDICINAL PRODUCTS AND OTHER FORMS OF INTERACTION
Drug-Drug Interactions: ROSUVASTATIN is known to contra-indicate when taken along with cyclosporine (organ transplants medicine), warfarin or clopidogrel (blood thinner), fibrates (gemfibrozil, fenofibrate), a medicine used to lower cholesterol (ezetimibe), antacid (aluminium hydroxide, magnesium hydroxide), antibiotics (erythromycin, fusidic acid), oral contraceptive pills, regorafenib (anti-cancer), anti-viral or anti-HIV drug (ritonavir, lopinavir, atazanavir, simeprevir, ombitasvir, paritaprevir, dasabuvir, velpatasvir, grazoprevir, elbasvir, glecaprevir, and pibrentsavir).
Drug-Food Interactions: Alcoholic beverages should be avoided with ROSUVASTATIN.
Drug-Disease Interactions: ROSUVASTATIN may interact with disease conditions, including neuromuscular disorders (Myopathy, Myoneural Disorder), thyroid gland problems (Hypothyroidism), and Renal Dysfunction.

PREGNACY, LACTATION & FERTILITY
Rosuvastatin is contraindicated in pregnancy and lactation.
Women of child bearing potential should use appropriate contraceptive measures.
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. Animal studies provide limited evidence of reproductive toxicity. 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.

EFFECTS ON ABILITY TO DRIVE AND USE MACHINES
Studies to determine the effect of Rosuvastatin on the ability to drive and use machines have not been conducted. However, based on its pharmacodynamic properties, Rosuvastatin is unlikely to affect this ability. When driving vehicles or operating machines, it should be taken into account that dizziness may occur during treatment.

UNDESIRABLE EFFECTS
Like all medicines, this medicine can cause side effects, although not everybody gets them.
It is important that you are aware of what these side effects may be. They are usually mild and disappear after a short time.
Stop taking rosuvastatin and seek medical help immediately if you have any of the following allergic reactions (rare side effects):
- Difficulty in breathing, with or without swelling of the face, lips, tongue and/or throat.
- Swelling of the face, lips, tongue and/or throat, which may cause difficulty in swallowing.
- Severe itching of the skin (with raised lumps).
- Lupus-like disease syndrome (including rash, joint disorders and effects on blood cells).
- Muscle rupture.
- Reddish non-elevated, target-like or circular patches on the trunk, often with central blisters, skin peeling, ulcers of mouth, throat, nose, genitals and eyes.
- These serious skin rashes can be preceded by fever and flu-like symptoms (Stevens-Johnson syndrome).
- Widespread rash, high body temperature and enlarged lymph nodes (DRESS syndrome or drug hypersensitivity syndrome).

Also, stop taking rosuvastatin and talk to your doctor immediately if you have any unusual aches or pains in your muscles which go on for longer than you might expect. Muscle symptoms are more common in children and adolescents than in adults. As with other statins, a very small number of people have experienced unpleasant muscle effects and rarely these have gone on to become a potentially life threatening muscle damage known as rhabdomyolysis (rare side effect).
Common possible side effects (may affect up to 1 in 10 people):
- Headache.
- Stomach pain.
- Constipation.
- Feeling sick.
- Muscle pain.
- Feeling weak.
- Dizziness.
- An increase in the amount of protein in the urine – this usually returns to normal on its own without having to stop taking your rosuvastatin tablets (only rosuvastatin 40 mg).
- Diabetes. This is more likely if you have high levels of sugars and fats in your blood, are overweight and have high blood pressure. Your doctor will monitor you while you are taking this medicine.

Uncommon possible side effects (may affect up to 1 in 100 people):
- Rash, itching or other skin reactions.
- An increase in the amount of protein in the urine – this usually returns to normal on its own without having to stop taking your rosuvastatin tablets (only Rosuvastatin 5 mg, 10 mg and 20 mg).

Rare possible side effects (may affect up to 1 in 1,000 people):
- Severe allergic reaction - signs include swelling of the face, lips, tongue and/or throat, difficulty in swallowing and breathing, a severe itching of the skin (with raised lumps). **If you think you are having an allergic reaction, then stop taking rosuvastatin** and seek medical help immediately.
- Muscle damage in adults - as a precaution, s**top taking rosuvastatin and talk to your doctor immediately if you have any unusual aches or pains** in your muscles which go on for longer than expected.
- A severe stomach pain (inflamed pancreas).
- Increase in liver enzymes in the blood.
- Decrease of platelets in the blood (thrombocytopenia).

Very rare possible side effects (may affect up to 1 in 10,000 people):
- Jaundice (yellowing of the skin and eyes).
- Hepatitis (an inflamed liver).
- Joint pain.
- Traces of blood in your urine.
- Damage to the nerves of your legs and arms (such as numbness).
- Memory loss.
- Breast enlargement in men (gynecomastia).

Side effects of unknown frequency may include (frequency cannot be estimated from the available data):
- Depression.
- Muscle weakness that is constant.
- Tendon injury.
- Sleep disturbances, including insomnia and nightmares.
- Diarrhoea (loose stools).
- Cough.
- Shortness of breath.
- Oedema (swelling).
- Sexual difficulties
- Breathing problems including persistent cough and/or shortness of breath or fever

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. Haemodialysis is unlikely to be of benefit.

INCOMPATIBILITY:
Not applicable.

SHELF LIFE:
36 months

PACKAGING
10 Tablets are packed in Alu-Alu blister; such 1 blister is packed in a printed monocarton along with pack insert; such 10 monocartons are packed in printed outer carton.

STORAGE:
Store at a temperature below 30^{0}C. Protect from direct sunlight, heat and moisture.
Keep the medicine out of reach of children.

MARKETED BY:
Pharma Wisdom

MANUFACTURED BY:
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