Rosatin®

Rosuvastatin

Film coated tablets 5, 10, 20 & 40 mg

Presentation:
Rosatin® 5: Each Film coated tablet contains 5mg Rosuvastatin (as Calcium Salt) in packs of 30 tablets.
Rosatin® 10: Each Film coated tablet contains 10mg Rosuvastatin (as Calcium Salt) in packs of 30 tablets.
Rosatin® 20: Each Film coated tablet contains 20mg Rosuvastatin (as Calcium Salt) in packs of 30 tablets.
Rosatin® 40: Each Film coated tablet contains 40mg Rosuvastatin (as Calcium Salt) in packs of 30 tablets.
Excipients: Lactose monohydrate, Calcium Carbonate, Microcrystalline Cellulose, Crospovidone, Magnesium Stearate, Opadry II White, Red Iron Oxide.
Pharmaceutical form:
Film coated tablet for oral use.
Pharmacotherapeutic group:
HMG-CoA reductase inhibitors, ATC code: C10A A07
Therapeutic Indications:
Rosatin® is indicated for the
Treatment of hypercholesterolemia:
- Adults, adolescents and children aged 10 years or older with primary hypercholesterolemia (type IIa including heterozygous familial hypercholesterolemia) or mixed dyslipidemia (type IIb) as an adjunct to diet when response to diet and other non-pharmacological treatments (e.g. exercise, weight reduction) is inadequate.
- Homozygous familial hypercholesterolemia 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:
Before treatment with **Rosatin®**, 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.
Rosatin® may be given at any time of day, with or without food.
Treatment of hypercholesterolemia:
The recommended starting dose of **Rosatin®** is 5 mg or 10 mg orally given once daily in both statin naive and 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, if necessary. 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 hypercholesterolemia at high cardiovascular risk (in particular those with familial hypercholesterolemia), 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.
Pediatric population: Pediatric use should only be carried out by specialists.
Children and adolescents 10 to 17 years of age (boys Tanner Stage II and above, and girls who are at least 1 year post-menarche): In children and adolescents with heterozygous familial hypercholesterolemia the usual starting dose of **Rosatin®** is 5 mg daily. The usual dose range is 5-20 mg orally given once daily. Titration should be conducted according to the individual response and tolerability in pediatric patients, as recommended by the pediatric treatment recommendations. Children and adolescents should be placed on standard cholesterol-lowering diet before **Rosatin®** treatment initiation; this diet should be continued during **Rosatin®** treatment. Safety and efficacy of doses greater than 20 mg have not been studied in this population. The 40 mg tablet is not suitable for use in pediatric patients.
Children younger than 10 years: Experience in children younger than 10 years is limited to a small number of children (aged between 8 and 10 years) with homozygous familial hypercholesterolemia. Therefore, **Rosatin®** is not recommended to use in children younger than 10 years.
Use in the elderly: A starting 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 starting 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 **Rosatin®** 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. **Rosatin®** 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 **Rosatin®** 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.
Concomitant therapy: Rosuvastatin is a substrate of various transporter proteins. The risk of myopathy (including rhabdomyolysis) is increased when **Rosatin®** 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 **Rosatin®** therapy. In situations where co-administration of these medicinal products with **Rosatin®** is unavoidable, the benefit and the risk of concurrent treatment and **Rosatin®** dosing adjustments should be carefully considered.
Contra-indications:
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 transaminase elevation exceeding 3x 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 cyclosporine.
- 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.

Warnings and Precautions for use:
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. The reporting rate for serious renal events in post-marketing use is higher at the 40 mg dose. An assessment of renal function should be considered during routine follow-up of patients treated with a dose of 40 mg.
Skeletal muscle effects: Effects on skeletal muscle e.g. myalgia, myopathy and, rarely, rhabdomyolysis have been reported in rosuvastatin-treated patients with all doses and in particular with doses> 20 mg. Very rare cases of rhabdomyolysis have been reported with the use of Ezetimibe in combination with HMG-CoA reductase inhibitors. A pharmacodynamics interaction cannot be excluded and caution should be exercised with their combined use.
As with other HMG-CoA reductase inhibitors, the reporting rate for rhabdomyolysis associated with rosuvastatin in post-marketing use is higher at the 40 mg dose.
Creatine Kinase measurement: Creatine Kinase (CK) should not be measured following strenuous exercise or in the presence of a plausible alternative cause of CK increase which may confound interpretation of the result. If CK levels are significantly elevated at baseline (>5xULN) a confirmatory test should be carried out within 5 -7 days. If the repeated test confirms a baseline CK >5xULN, treatment should not be started.
Before treatment
Rosuvastatin, as with other HMG-CoA reductase inhibitors, should be prescribed with caution in patients with pre-disposing factors for myopathy/rhabdomyolysis. Such factors include: Renal impairment, 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 CK levels are significantly elevated at baseline (>5xULN) treatment should not be started,
Whilst on treatment
Patients should be asked to report inexplicable muscle pain, weakness or cramps immediately, particularly if associated with malaise or fever. CK levels should be measured in these patients. Therapy should be discontinued if CK levels are markedly elevated (>5xULN) or if muscular symptoms are severe and cause daily discomfort (even if CK levels are ≤5xULN). If symptoms resolve and CK levels return to normal, then consideration should be given to re-introducing rosuvastatin or an alternative HMG-CoA reductase inhibitor at the lowest dose with close monitoring.
Routine monitoring of CK levels in asymptomatic patients is not warranted.
There have been very rare reports of an immune-mediated necrotising myopathy (IMNM) during or after treatment with statins, including rosuvastatin. IMNM is clinically characterised by proximal muscle weakness and elevated serum creatine kinase, which persist despite discontinuation of statin treatment.
In clinical trials there was no evidence of increased skeletal muscle effects in the small number of patients dosed with rosuvastatin and concomitant therapy. However, an increase in the incidence of myositis and myopathy has been seen in patients receiving other HMG-CoA reductase inhibitors together with fibric acid derivatives including Gemfibrozil, cyclosporine, nicotinic acid, azole antifungals, protease inhibitors and macrolide antibiotics. Gemfibrozil increases the risk of myopathy when given concomitantly with some HMG-CoA reductase inhibitors. Therefore, the combination of rosuvastatin 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. The 40 mg dose is contraindicated with concomitant use of a fibrate.
rosuvastatin should not be used in any 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).
Liver effects: As with other HMG-CoA reductase inhibitors, rosuvastatin 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. The reporting rate for serious hepatic events (consisting mainly of increased hepatic transaminases) in post-marketing use is higher at the 40 mg dose. In patients with secondary hypercholesterolemia caused by hypothyroidism or nephrotic syndrome, the underlying disease should be treated prior to initiating therapy with rosuvastatin.
Race: Pharmacokinetic studies show an increase in exposure in Asian subjects compared with Caucasians.
Protease inhibitors: Increased systemic exposure to rosuvastatin has been observed in subjects receiving rosuvastatin concomitantly with various protease inhibitors in combination with ritonavir. Consideration should be given both to the benefit of lipid lowering by use of rosuvastatin in HIV patients receiving protease inhibitors and the potential for increased rosuvastatin plasma concentrations when initiating and up titrating rosuvastatin doses in patients treated with protease inhibitors. The concomitant use with certain protease inhibitors is not recommended unless the dose of rosuvastatin is adjusted.
Lactose intolerance: Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.
Interstitial lung disease: Exceptional cases of interstitial lung disease have been reported with some statins, especially with long term therapy. Presenting features can include dyspnea, non-productive cough and deterioration in general health (fatigue, weight loss and fever). If it is suspected a patient has developed interstitial

lung disease, statin therapy should be discontinued.

Diabetes Mellitus: As with other HMG-CoA reductase inhibitors, increases in HbA1c and serum glucose levels have been observed in patients treated with rosuvastatin., and in some instances these increases may exceed the threshold for the diagnosis of diabetes mellitus, primarily in patients already at high risk for developing diabetes.

Pediatric population: The evaluation of linear growth (height), weight, BMI (body mass index), and secondary characteristics of sexual maturation by Tanner staging in pediatric patients 10 to 17 years of age taking Rosuvastatin is limited to a one-year period. After 52 weeks of study treatment, no effect on growth, weight, BMI or sexual maturation was detected. The clinical trial experience in children and adolescent patients is limited and the long-term effects of Rosuvastatin (>1 year) on puberty are unknown.

In a clinical trial of children and adolescents receiving Rosuvastatin for 52 weeks, CK elevations> 10xULN and muscle symptoms following exercise or increased physical activity were observed more frequently compared to observations in clinical trials in adults.

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.

Use During pregnancy and lactation:

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 fetus, 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.

Drug Interactions:

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.

Cyclosporine: During concomitant treatment with rosuvastatin and cyclosporine, Rosuvastatin AUC values were on average 7 times higher than those observed in healthy volunteers. Concomitant administration did not affect plasma concentrations of cyclosporine.

Ezetimibe: Concomitant use of rosuvastatin and Ezetimibe resulted in no change to C_{max} or AUC for either drug. However, a Pharmacodynamic interaction, in terms of adverse effects, between rosuvastatin and Ezetimibe cannot be ruled out.

Gemfibrozil and other lipid-lowering products: Concomitant use of rosuvastatin and Gemfibrozil resulted in a 2-fold increase in Rosuvastatin C_{max} and AUC. Based on data from specific interaction studies no pharmacokinetic relevant interaction with Fenofibrate is expected, however a Pharmacodynamic interaction may occur. Gemfibrozil, fenofibrate, other fibrates and lipid lowering doses (> or equal to 1 g/day) of niacin (nicotinic acid) increase the risk of myopathy when given concomitantly with HMO-CoA reductase inhibitors, probably because they can produce myopathy when given alone. The 40 mg dose is contraindicated with concomitant use of a fibrate. These patients should also start with the 5 mg dose.

Protease inhibitors: Although the exact mechanism of interaction is unknown, concomitant protease inhibitor use may strongly increase Rosuvastatin exposure, the concomitant use with protease inhibitors is not recommended. In a pharmacokinetic study, co-administration of 20 mg Rosuvastatin and a combination product of two protease inhibitors (400 mg lopinavir /100 mg ritonavir) in healthy volunteers was associated with an approximately Iwo-foid and five-fold increase in Rosuvastatin steady-state AUC (0-24) and C_{max} respectively. Therefore, concomitant use of Rosuvastatin in HIV patients receiving protease inhibitors is not recommended.

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%. This effect was mitigated when the antacid was dosed 2 hours after rosuvastatin. The clinical relevance of this interaction has not been studied.

Erythromycin: 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.

Cytochrome P450 enzymes: Results from in vitro and in vivo studies show that Rosuvastatin is neither an inhibitor nor an inducer of cytochrome P450 isoenzymes. In addition, Rosuvastatin is a poor substrate for these isoenzymes. No clinically relevant interactions have been observed between Rosuvastatin and either fluconazole (an inhibitor of CYP2C9 and CYP3A4) or ketoconazole (an inhibitor of CYP2A6 and CYP3A4).

Concomitant administration of itraconazole (an inhibitor of CYP3A4) and Rosuvastatin resulted in a 28% increase in AUC of Rosuvastatin. This small increase is not considered clinically significant. Therefore, drug interactions resulting from cytochrome P450-mediated metabolism are not expected.

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 (AVC) 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.

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 Normalized 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. However, the combination has been extensively used in women in clinical trials and was well tolerated.

Other medicinal products: Based on data from specific interaction studies no clinically relevant interactions with digoxin are expected.

Paediatric population: Interaction studies have only been performed in adults. The extent of interactions in the paediatric population is not known.

Undesirable effects:

The adverse events seen with rosuvastatin are generally mild and transient. In controlled clinical trials, less than 4% of rosuvastatin-treated patients were withdrawn due to adverse events.

Common: Diabetes mellitus, headache, dizziness, constipation, nausea, abdominal pain, myalgia and asthenia.

Rare: Thrombocytopenia, hypersensitivity reactions including angioedema, pancreatitis, increased hepatic transaminases, pruritus, rash, urticaria, myopathy (including myositis) and rhabdomyolysis.

Very rare: Polyneuropathy, memory loss, jaundice, hepatitis, arthralgia, haematuria and gynaecomastia.

Not known: Depression, sleep disturbances (including insomnia and nightmares), cough, dyspnoea, diarrhea, stevens-Johnson syndrome, immunemediated necrotising myopathy and oedema.

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 <1 % of patients at some time during treatment with 10 and 20 mg, and in approximately 3% of patients treated with 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. Review of data from clinical trials and post-marketing experience to date has not identified a causal association between proteinuria and acute or progressive renal disease. Hematuria has been observed in patients treated with rosuvastatin and clinical trial data show that the occurrence is low.

Skeletal muscle effects: Effects on skeletal muscle e.g. myalgia, myopathy (including myositis) and, rarely, 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; the majority of cases were mild, asymptomatic and transient. 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 a small number of patients taking Rosuvastatin; the majority of cases were mild, asymptomatic and transient.

The following adverse events have been reported with some statins:

Sexual dysfunction, exceptional cases of interstitial lung disease, especially with long term therapy, the reporting rates for rhabdomyolysis, serious renal events and serious hepatic events (consisting mainly of increased hepatic transaminases) is higher at the 40 mg dose.

Paediatric population: Creatine kinase elevations >10xULN and muscle symptoms following exercise or increased physical activity were observed more frequently in a 52-week clinical trial of children and adolescents compared to adults. In other respects, the safety profile of rosuvastatin was similar in children and adolescents compared to adults.

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.

Pharmacodynamic properties

Rosatin® (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.

Pharmacokinetic properties

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.

Metabolism: 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.

Excretion: Approximately 90% of the Rosuvastatin dose is excreted unchanged in the feces (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 liters/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.

Linearity: Systemic exposure of Rosuvastatin increases in proportion to dose. There are no changes in pharmacokinetic parameters following multiple daily doses.

Special precautions for storage:

Store below 30°C.

Feb., 2014
I-Rosatin-RSN-LM0-R0/EE

This is a medicament

- A medicament is a product which affects your health, and its consumption contrary to instructions is dangerous for you.
- Follow strictly the doctor's prescription, the method of use and the instructions of the pharmacist who sold the medicament.
- The doctor and the pharmacist are experts in medicine, its benefits and risks.
- Do not by yourself interrupt the period of treatment prescribed for you.
- Do not repeat the same prescription without consulting your doctor.
- Keep medicament out of the reach of children.

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