Rx Thuốc bán theo đơn

CRESTOR®

5 mg; 10 mg; 20 mg
Rosuvastatin calci
Viên nén bao phim

MẪU QUẢNG CÁO DÀNH CHO BÁC SĨ
THÔNG TIN SẢN PHẨM TÓM TẮT
THÔNG TIN CẦN THIẾT CHO LÂM SÀNG TRƯỚC KHI DÙNG THUỐC

P05066

THÀNH PHẦN VÀ HÀM LƯỢNG

Thành phần hoạt chất: Mỗi viên chứa 5 mg, 10 mg, 20 mg rosuvastatin dưới dạng rosuvastatin calci.
Thành phần tá dược:
Thành phần viên nhân: lactose monohydrat, cellulose vi tinh thể, calci phosphat, croscarmellose, magnesi stearat.
Thành phần bao viên: hypromellose, hypromellose, glycerol triacetat, titan dioxyd (E171), sắt oxyd vàng (E172).

DẠNG BÀO CHẾ

Viên nén bao phim.
Viên nhân màu vàng 5 mg; hình tròn, mặt trên nhẵn, không 10 mg và 20 mg.

CHỈ ĐỊNH ĐIỀU TRỊ

Bổ sung cho chế độ ăn hạn chế cholesterol và chế độ ăn giảm cholesterol khi chế độ ăn hạn chế cholesterol và chế độ ăn giảm cholesterol là thích hợp để làm chậm tiến triển xơ vữa động mạch ở những bệnh nhân không đáp ứng đầy đủ với chế độ ăn kiểng và các biện pháp không dùng thuốc khác là thích hợp để thay thế cho chế độ ăn.

Rối loạn lipid lượng/chất máu nguyên phát (typa IIa/phenotypa mixtus typ IIb): CRESTOR được chỉ định cho trị liệu thay thế cho chế độ ăn uống hiện tại ở những bệnh nhân có nguy cơ tim mạch cao phù hợp với chỉ định của điều trị bổ sung cho chế độ ăn kiểng.

Phòng ngừa biến cố tim mạch: CRESTOR được chỉ định cho những bệnh nhân người trưởng thành không biểu hiện lâm sàng bệnh tim mạch nhưng có nguy cơ tim mạch cao phù hợp với chỉ định của điều trị bổ sung cho chế độ ăn kiểng.

Bệnh nhân từ 7 đến 17 tuổi bị rối loạn lipid lượng/chất máu nguyên phát gồm thể kiểu dạng hỗn tạp (typa IIa) hoặc thể kiểu dạng hỗn tạp (typa IIb) được chẩn đoán theo phân loại Fredrick, mức nhóm bệnh có thể phù hợp với CRESTOR được xem là:

Bệnh nhân từ 8 đến 17 tuổi bị tăng cholesterol máu gia đình kiểu dị hợp tử (HeFH): Mỗi bữa ăn chế độ ăn kiểng nhằm làm giảm lượng cholesterol tiêu thụ phù hợp với chỉ định của điều trị bổ sung cho

Rx Prescription only medicine

CRESTOR®

5 mg, 10 mg, 20 mg
Rosuvastatin calcium
Film-Coated Tablets

WHAT IS AND WHAT DOES IT MEAN FOR YOU

PRESCRIPTION ONLY MEDICINE

COMPOSITION AND STRENGTH

Active ingredients: Each tablet contains 5 mg, 10 mg, 20 mg of rosuvastatin as rosuvastatin calcium.

Excipients:

Tablet core: lactose monohydrate, microcrystalline cellulose, calcium phosphate crospovidone, magnesium stearate.

Tablet coat: lactose monohydrate, hypromellose, glycerol triacetate, titanium dioxide (E171), ferric oxide, yellow (E172).

PHARMACEUTICAL DOSAGE FORM

Film-coated tablet.

Round, yellow coloured (5 mg); round, pink coloured (10 mg and 20 mg).

THERAPEUTIC INDICATIONS

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.

Primary Dysbetalipoproteinemia (Type III Hyperlipoproteinemia): CRESTOR is indicated as an adjunct to diet for the treatment of patients with primary dysbetalipoproteinemia (Type III Hyperlipoproteinemia).

CRESTOR is indicated as adjunctive therapy to diet for the treatment of adult patients with hypertriglyceridemia.

Pediatric Patients 7 to 17 years of age and adults with homozygous familial hypercholesterolemia to reduce LDL-C and Apo B levels in children and adolescent 8-17 years of age with heterozygous familial hypercholesterolemia if after an adequate trial of diet therapy the following criteria are met: LDL-C > 190 mg/dL or, > 160 mg/dL and along with a positive family history of premature cardiovascular disease (CVD) or two or more other CVD risk factors.

CRESTOR is indicated as adjunctive therapy to diet to slow the progression of atherosclerosis in adult patients as part of a treatment strategy to lower Total-C and LDL-C to target levels.

Primary Prevention of Cardiovascular Disease:

In individuals without clinically evident coronary heart disease but with an increased risk of cardiovascular disease based on age ≥ 50 years old in men and ≥ 60 years old in women with at least one CVD risk factor, CRESTOR is indicated to reduce one additional cardiovascular disease risk factor such as hypertension, low HDL-C, smoking, or a family history of premature coronary heart disease, CRESTOR is indicated for:

- reduce the risk of stroke
- reduce the risk of myocardial infarction
- reduce the risk of arterial revascularization procedures

Limitations of Use: CRESTOR has not been studied in Fredrickson Type I and V dyslipidemias.

POSOLOGY AND METHOD OF ADMINISTRATION

Treatment should be initiated with diet, and should be based on a standard cholesterol-lowering diet that should continue during treatment. The dosage should be individualized according to the goal of therapy and patient response, using current clinical guidelines.

Crestor may be given at any time of day with or without food.

Treatment of hypercholesterolemia

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 be based on the patient's cholesterol level and future cardiovascular disease risk as well as the potential risk for adverse reactions. A dose adjustment to the next dose level can be made after 4 weeks to achieve the goal. The maximum dose with low rate of adverse reactions with the 40 mg dose should be considered in patients with severe hypercholesterolemia at high cardiovascular risk who do not achieve their lipid hypercholesterolemia), who do not achieve their treatment goal on 20 mg, and in whom safety and vigilance is 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 use

In heterozygous familial hypercholesterolemia: the recommended dose range is 5 to 10 mg orally once daily in patients 8 to less than 10 years of age, and 5 to 20 mg orally once daily in patients 10 to 17 years of age.

In homozygous familial hypercholesterolemia: the recommended dose is 20 mg orally once daily in patients 7 to 17 years of age.

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.

Dosing in patients with renal insufficiency

In patients with renal impairment (patients with mild to moderate renal impairment, The recommended start dose is 5 mg orally once daily. The dose of CRESTOR should not exceed 10 mg once daily (see *Special warnings and precautions for use* and *Pharmacokinetic properties*).

Initiate CRESTOR therapy with 5 mg once daily. The dose of CRESTOR should not exceed 10 mg once daily (see *Special warnings and precautions for use* and *Pharmacokinetic properties*).

CONTRAINDICATIONS

Crestor is contraindicated:

- in patients with hypersensitivity to rosuvastatin or to any of the excipients.
- in patients with severe renal impairment (creatinine clearance <30 mL/min), serum transaminases and any serum transaminase elevation exceeding 3 x 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 cyclosporin.
- 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 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 Crestor, in particular 40 mg, where it was transient or intermittent in most cases. Proteinuria has been shown to be predictive of acute or progressive renal disease (see Undesirable effects). 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 Crestor-treated patients with all doses and particular with doses > 20 mg.

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 repeat test confirms a baseline CK >5xULN, treatment should not be started.

Before Treatment

Crestor, as with other HMG-CoA reductase inhibitors having risk of causing adverse muscle effects, should be prescribed with caution in patients with risk factors predisposing for myopathy/rhabdomyolysis. CK should be measured in the following circumstances:

- renal impairment
- hypothyroidism
- personal or family history of hereditary muscular disorders
- previous history of muscular disorders associated with statin and fibrate use
- previous history of muscular toxicity with another HMG-CoA reductase inhibitor or fibrate
- elderly patients age > 70 years with pre-disposing factors for rhabdomyolysis
- situations where an increase in plasma levels may occur (see Pharmacokinetic properties)
- concomitant use of fibrates
- situations where drug interactions may occur and in some special populations

In such circumstances the risk of treatment should be considered in relation to possible benefit and clinical monitoring is recommended when treated with statin. If CK levels are significantly elevated (>5xULN) at baseline, treatment should not be started.

While on Treatment

Closely monitor adverse reactions during drug therapy. Patients should be asked to report to their doctor's manifestations of muscle pain, muscle rigidity, weakness or cramps immediately, particularly if associated with malaise, fever, dark urine, nausea or vomiting during drug therapy. If these symptoms occur, CK levels should be measured in order to take appropriate interventions. Therapy should be discontinued if CK levels are significantly elevated (>5xULN). If muscle symptoms are severe and cause daily discomfort (even if CK levels are ≤ 5x ULN), if symptoms persist and CK levels return to normal, then consideration should be given to re-introducing Crestor or another HMG-CoA reductase inhibitor at the lowest dose and with close monitoring.

Crestor should be used with caution if predisposing factors are present.

Crestor Rhabdomyolysis

Treatment with Crestor 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 repeat test confirms a baseline CK >5xULN, treatment should not be started.

Before Treatment

Crestor, as with other HMG-CoA reductase inhibitors having risk of causing adverse muscle effects, should be prescribed with caution in patients with risk factors predisposing for myopathy/rhabdomyolysis. CK should be measured in the following circumstances:

- renal impairment
- hypothyroidism
- personal or family history of hereditary muscular disorders
- previous history of muscular disorders associated with statin and fibrate use
- previous history of muscular toxicity with another HMG-CoA reductase inhibitor or fibrate
- elderly patients age > 70 years with pre-disposing factors for rhabdomyolysis
- situations where an increase in plasma levels may occur (see Pharmacokinetic properties)
- concomitant use of fibrates
- situations where drug interactions may occur and in some special populations

In such circumstances the risk of treatment should be considered in relation to possible benefit and clinical monitoring is recommended when treated with statin. If CK levels are significantly elevated (>5xULN) at baseline, treatment should not be started.

Whilst on Treatment

Closely monitor adverse reactions during drug therapy. Patients should be asked to report to their doctor's manifestations muscle pain, muscle rigidity, weakness or cramps immediately, particularly if associated with malaise, fever, dark urine, nausea or vomiting during drug therapy. If these symptoms occur, CK levels should be measured in order to take appropriate interventions. Therapy should be discontinued if CK levels are significantly elevated (>5xULN). If muscle symptoms are severe and cause daily discomfort (even if CK levels are ≤ 5x ULN), if symptoms persist and CK levels return to normal, then consideration should be given to re-introducing Crestor or another HMG-CoA reductase inhibitor at the lowest dose and with close monitoring.

Crestor with fibrates or cyclosporin should be used with caution.

Crestor Myopathy

Myopathy has been reported with all HMG-CoA reductase inhibitors, the initiation of treatment, and during subsequent follow-up, should be carefully considered in patients at risk for myopathy when given concomitantly with some HMG-CoA reductase inhibitors, for example, the combination of Crestor and gemfibrozil is not recommended. Myopathy has been reported in clinical trials with Crestor and in the post-marketing period. Myopathy has been reported with Crestor with fibrates and/or cyclosporin and should not take this medicine.

Pediatric Use

In children and adolescents 8 to 17 years of age with heterozygous familial hypercholesterolemia, the safety and effectiveness of CRESTOR are not established. Data are limited in children 7 to 17 years of age with homozygous familial hypercholesterolemia. The safety and effectiveness of CRESTOR in children and adolescents 10 to 17 years of age with heterozygous familial hypercholesterolemia are supported by a controlled trial with a dose duration followed by 42 weeks of open-label exposure. Patients treated with 5 mg, 10 mg, and 20 mg daily for 12 weeks and an extension to 52 weeks generally similar to the adult safety profile in adults. There was no detectable effect on CRESTOR on growth, weight, BMI (body mass index), or sexual maturation in children and adolescents 10 to 17 years of age.

CRESTOR has not been studied in controlled clinical trials involving prepubertal patients less than younger than 10 years of age with homozygous familial hypercholesterolemia. However, the safety and effectiveness of CRESTOR were evaluated in a two year open-label, uncontrolled, dose-titration study in 8 to less than 10 years of age with homozygous familial hypercholesterolemia. The safety and efficacy of CRESTOR in lowering LDL-C appeared generally consistent with that observed for adult patients despite limitations of the uncontrolled study design.

Children and adolescents 7 to 15 years of age with homozygous familial hypercholesterolemia treated with 20 mg once daily CRESTOR in a placebo-controlled, cross-over study with CRESTOR 20 mg once daily followed by 12 weeks of open-label treatment. Results were consistent with the known safety profile of CRESTOR in previously established safety profile in adults.

Although not all adverse reactions identified in the adult population have been observed in clinical trials of children and adolescent patients, the same warnings and precautions for adults should be considered for children and adolescents. Adolescent females should be counseled on appropriate methods of contraception and pregnancy.

INTERACTION WITH OTHER MEDICINAL PRODUCTS AND OTHER FORMS OF INTERACTION

Effect of co-administered medicinal products on rosuvastatin

Transporter protein (OATP1B1 and BCRP) mediated uptake is a certain transporter protein including the hepatocyte transporter protein organic anion transporter (OSP) Concomitant administration of Crestor with medicinal products that are inhibitors of these transporter proteins may result in increased rosuvastatin concentrations and an increased risk of myopathy (see *Posology and method of administration, Special warnings and precautions for use* and *Interactions with other medicinal products and other forms of interaction*: Table 1).

Rosuvastatin is not a concomitant treatment with Crestor and cyclosporine, rosuvastatin AUC values were on average 7 times higher than those observed in healthy volunteers (see Table 1). Crestor is contraindicated in patients receiving concomitant cyclosporin.

Concomitant administration of rosuvastatin and medicinal products that increase Protease Inhibitor: Although the exact mechanism of interaction is unknown, concomitant protease inhibitor use may strongly increase rosuvastatin exposure (see Table 1). For instance, in a pharmacokinetic study, co-administration of 10 mg rosuvastatin and a combination product containing 2 protease inhibitors (300 mg atazanavir / 100 mg ritonavir) in healthy volunteers was associated with a 3-fold increase in rosuvastatin AUC and a three-fold and seven-fold increase in rosuvastatin AUC and Cmax respectively. The combination of rosuvastatin and some protease inhibitors combinations may be considered after careful consideration of Crestor dose adjustments based on the expected increase in rosuvastatin exposure (see *Posology and method of administration, Special warnings and precautions for use* and *Interactions with other medicinal products and other forms of interaction* - Table 1).

Gemfibrozil and other lipid lowering products: Use of Crestor and gemfibrozil resulted in a 2-fold increase in rosuvastatin Cmax and AUC (see *Special warnings and precautions for use*).

Based on data from specific interaction studies, no interaction is expected between fenofibrate is expected, however a pharmacokinetic interaction may occur. Gemfibrozil, cyclosporine, and other fibrates and lipid-lowering (≥ or equal to 1g/day) of niacin (nicotinic acid) increase the risk of myopathy when given concomitantly with HMG-CoA reductase inhibitors, presumably because they produce myopathy when given alone. The 40 mg dose is contraindicated with gemfibrozil and fibrates (see Contraindications and Special warnings and precautions for use). These fibrates also start with the 5 mg dose.

Coumarins

Concomitant use of 10 mg Crestor and 10 mg ezetimibe resulted in a 1.2 fold increase in AUC of rosuvastatin in hypercholesterolemic subjects (Table 1). A pharmacodynamic interaction, in terms of adverse effects, between Crestor and coumarins cannot be ruled out.

Antacid

The simultaneous dosing of Crestor with an antacid suspension containing aluminum and magnesium hydroxides, resulted in a decrease in rosuvastatin plasma concentration of approximately 50%. This effect was mitigated when the antacid was dosed 2 hours after Crestor. The clinical relevance of this interaction has not been studied.

Erythromycin

Concomitant use of Crestor and erythromycin resulted in a 20% decrease in AUC and a 31% decrease in Cmax of rosuvastatin. This interaction may be caused by the increase in gut motility caused by erythromycin.

Dihydrofolate PRO enzyme

Results from in vitro and in vivo studies show that rosuvastatin is neither an inhibitor nor an substrate for human dihydrofolate reductase, a enzyme that is responsible for the biosynthesis. Therefore, drug interactions resulting from cytochrome P450-mediated metabolism are not expected. No significant drug interactions have been observed between rosuvastatin and either fluconazole (an inhibitor of CYP2C9 and CYP3A) and ketoconazole (an inhibitor of CYP2A6 and CYP3A).

Interactions requiring dose adjustments of rosuvastatin (see Table 1):

When it is necessary to co-administer Crestor with other medicinal products known to increase the plasma concentrations of rosuvastatin, the dose of Crestor should be adjusted. Start with a 5 mg dose daily dose of Crestor if the expected increase in exposure (AUC) is approximately 2-fold or higher. The maximum daily dose of Crestor should be adjusted so that the expected rosuvastatin exposure would not be higher than a 5 mg daily dose of Crestor taken without interacting medicinal products, for example a 20 mg dose of Crestor with gemfibrozil (1.9-fold increase), and 10 mg dose of Crestor with combination rosuvastatinamide (3-fold increase).

Table 1: Effect of co-administered medicinal products on rosuvastatin exposure (AUC; in order of decreasing magnitude) from published clinical trials

Interacting drug dose regimen	Rosuvastatin dose regimen	Change in rosuvastatin AUC*
Ciclosporin 75 mg BID to 200 mg BID, 6 months	10 mg OD, 10 days	7.1-fold↑
Atazanavir 300 mg/ritonavir 100 mg OD, 8 days	10 mg, single dose	3.1-fold↑
Simeprevir 150 mg OD, 7 days	10 mg, single dose	2.8-fold↑
Lopinavir 400 mg/ritonavir 100 mg BID, 17 days	20 mg OD, 7 days	2.1-fold↑
Ciprofloxacin 500 mg loading, followed by 75 mg of 24 hours	20 mg, single dose	2.0fold↑
Gemfibrozil 600 mg BID, 7 days	80 mg, single dose	1.9-fold↑
Eltrombopag 75 mg OD, 5 days	10 mg, single dose	1.6-fold↑
Darunavir 600 mg/ritonavir 100 mg BID, 7 days	10 mg OD, 7 days	1.5-fold↑
Darunavir 600 mg/ritonavir 100 mg BID, 11 days	10 mg, single dose	1.4-fold↑
Dronedarone 400 mg BID	Not recorded	1.4-fold↑
Ivacaxone 200 mg OD, 5 days	10 mg, single dose	**1.4-fold ↑**
Fosaprepitant 150 mg, 1 dose	10 mg OD, 14 days	**1.3-fold ↑**
Fosamprenavir 700 mg/ritonavir 100 mg BID, 8 days	10 mg, single dose	**
Aleglitazar 0.3 mg, 7 days	40 mg, 7 days	**
Silymarin 140 mg BID, 5 days	10 mg, single dose	**
Fenofibrate 67 mg TID, 7 days	10 mg, 7 days	**
Rilmapin 450 mg OD, 7 days	20 mg, single dose	**
Ketoconazole 200 mg BID, 5 days	80 mg, single dose	**
Fluconazole 200 mg OD, 11 days	80 mg, single dose	**
Erythromycin 500 mg QID, 7 days	80 mg, single dose	20% ↓
Baicalin 50 mg TID, 14 days	20 mg, single dose	47% ↓

*Data given as a fold change represent a simple ratio between co-administration and rosuvastatin alone. Data given as a % change represent a different ratio to rosuvastatin alone.

**Arrows indicated as ↑↑, no change as "↔", decrease as "↓".

***General interaction not have been performed at different Crestor dosages, the table shows the most significant ratio.

BID = twice daily; TID = three daily; QID = four times daily; OD = four times daily

Effect of rosuvastatin on co-administered medicinal products

Vitamin K antagonists: Like other HMG-CoA reductase inhibitors, the initiation of treatment or dosage up-titration of Crestor in patients concomitantly taking other 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 Crestor may result in a decrease in INR. In such circumstances, appropriate INR monitoring is possible. Oral contraceptive/hormone replacement therapy (HRT)

Co-administration of Crestor and oral contraceptives resulted in an increase in ethinyl estradiol and norgestrel AUC of 26% and 11%, respectively. These increase plasma levels should be considered when selecting oral contraceptive products for a woman taking pharmacokinetic data available with rosuvastatin combination Crestor 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

Rosuvastatin does not have specific interaction studies no clinically relevant interaction with digoxin is expected.

Fusidic Acid: Interaction studies with rosuvastatin and fusidic acid have not been conducted. As with other statins, muscle related events, including rhabdomyolysis, have been reported. Post-marketing experience with rosuvastatin and fusidic acid given concurrently. Therefore, the combination is not recommended. If treatment with fusidic acid is possible, temporary suspension of rosuvastatin treatment is recommended. If unavoidable, patients should be closely monitored.

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

PREGNANCY AND LACTATION

Crestor 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 risk of drug-induced fetal harm is considered to outweigh the advantages 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.

Animal studies have shown toxicity to the fetus. There are no data with respect to excretion in milk in humans (see *Contraindications*).

EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

Studies to determine the effect of Crestor on the ability to drive and use machines have not been conducted. However, based on its pharmacodynamic profile, Crestor 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

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

Tabulated list of adverse reactions

Based on data from clinical studies and extensive post-marketing experience, the following table presents the adverse reaction profile for rosuvastatin. Adverse reactions listed below are classified according to frequency and system organ class.

The frequencies of adverse reactions are defined as follows: Common (≥1/100 to <1/10); Uncommon (≥1/1000 to <1/100); Rare (≥1/10,000 to <1/1000); Very rare (<1/10,000); Not known (cannot be estimated from the available data).

System organ class	Common	Uncommon	Rare	Very rare	Not known
Blood and lymphatic system disorders			Thrombocytopenia		
Immune system disorders			Hypersensitivity reactions including angioedema		
Endocrine disorders	Diabetes Mellitus				
Psychiatric disorders					Depression
Nervous system disorders	Headache, Dizziness			Polyneuropathy, Memory loss	Peripheral neuropathy, Sleep disturbances (including insomnia and nightmares)
Respiratory, thoracic and mediastinal disorders			Cough		Cough, Dyspnoea
Gastro-intestinal disorders	Constipation, Nausea, Abdominal pain		Pancreatitis		Diarrhoea
Hepatobiliary disorders				Jaundice, Hepatitis	
Skin and subcutaneous tissue disorders		Pruritic, Rash, Urticaria			Drug Rash with Eosinophilia and Systemic Symptoms, Stevens Johnson syndrome
Musculoskeletal and connective tissue disorders	Myalgia		Myopathy (including myositis), Rhabdomyolysis	Arthralgia	Tendon disorders, sometimes complicated by rupture, Arthropathy, Muscle cramps, Immune mediated musculoskeletal disorders
Renal and urinary disorders				Haematuria	
Reproductive system and breast disorders				Gynaecomastia	
General disorders and administration site conditions	Asthenia				Oedema

Frequency will depend on the presence or absence of risk factors (fading blood disorder a CK increase, BMI ≥25 kg/m², renal impairment, history of myopathy).

Rosuvastatin is an HMG-CoA reductase inhibitor, 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 Crestor. Shifts in urine protein from none or trace to 1+ or more were seen in <1% of patients at some time during treatment with 5 mg and 10 mg, and in approximately 3% of patients treated with 40 mg. A minor increase in shift from none or trace to 1+ was observed with 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 worsening of progressive renal disease.

Haematuria has been observed in patients treated with Crestor and clinical trial data show that it is uncommon in nature.

Skeletal muscle effects: Effects on skeletal muscle e.g. myalgia, myopathy (including myositis), and, rarely rhabdomyolysis have been reported in patients with all doses and particular with doses > 20 mg and in patients with a predisposition for myopathy.

A dose-related increase in CK levels has been observed in patients taking rosuvastatin; the majority of cases are mild and asymptomatic. If elevated CK levels (> 5 x upper limit of normal (ULN)), treatment should be discontinued (see *Special warnings and precautions for use*).

Rosuvastatin has been associated with an increased risk of myopathy when given concomitantly with a fibrate. Rosuvastatin has been observed in a small number of patients taking rosuvastatin; the majority of cases are mild and asymptomatic.

Hepatic effects: Like other HMG-CoA reductase inhibitors, Crestor should be used with caution in patients consuming alcohol and/or have a history of liver disease. Liver function tests should be performed when clinically indicated. Rosuvastatin