5.3 Hepatic Dysfunction

Increases in serum transaminases have been reported with use of CRESTOR *[see Adverse Reactions (6.1)]*. In most cases, these changes appeared soon after initiation, were transient, were not accompanied by symptoms, and resolved or improved on continued therapy or after a brief interruption in therapy. In a pooled analysis of placebo-controlled trials, increases in serum transaminases to more than three times the ULN occurred in 1.1% of patients taking CRESTOR versus 0.5% of patients treated with placebo. Marked persistent increases of hepatic transaminases have also occurred with CRESTOR. There have been rare postmarketing reports of fatal and non-fatal hepatic failure in patients taking statins, including CRESTOR.

Patients who consume substantial quantities of alcohol and/or have a history of liver disease may be at increased risk for hepatic injury *[see Use in Specific Populations (8.7)]*.

Consider liver enzyme testing before CRESTOR initiation and when clinically indicated thereafter. CRESTOR is contraindicated in patients with acute liver failure or decompensated cirrhosis *[see Contraindications (4)]*. If serious hepatic injury with clinical symptoms and/or hyperbilirubinemia or jaundice occurs, promptly discontinue CRESTOR.

5.4 Proteinuria and Hematuria

In the CRESTOR clinical trial program, dipstick-positive proteinuria and microscopic hematuria were observed among CRESTOR treated patients. These findings were more frequent in patients taking CRESTOR 40 mg, when compared to lower doses of CRESTOR or comparator statins, though it was generally transient and was not associated with worsening renal function. Although the clinical significance of this finding is unknown, consider a dose reduction for patients on CRESTOR therapy with unexplained persistent proteinuria and/or hematuria during routine urinalysis testing.

5.5 Increases in HbA1c and Fasting Serum Glucose Levels

Increases in HbA1c and fasting serum glucose levels have been reported with statins, including CRESTOR. Based on clinical trial data with CRESTOR, in some instances these increases may exceed the threshold for the diagnosis of diabetes mellitus *[see Adverse Reactions (6.1)]*. Optimize lifestyle measures, including regular exercise, maintaining a healthy body weight, and making healthy food choices.

6 ADVERSE REACTIONS

The following important adverse reactions are described below and elsewhere in the labeling:

Myopathy and Rhabdomyolysis *[see Warnings and Precautions (5.1)]*
Immune-Mediated Necrotizing Myopathy *[see Warnings and Precautions (5.2)]*
Hepatic Dysfunction *[see Warnings and Precautions (5.3)]*
Proteinuria and Hematuria *[see Warnings and Precautions (5.4)]*

In the JUPITER study, patients were treated with CRESTOR 20 mg (n=8901) or placebo (n=8901) for a mean duration of 2 years. In JUPITER, there was a significantly higher frequency of diabetes mellitus reported in patients taking CRESTOR (2.8%) versus patients taking placebo (2.3%). Mean HbA1c was significantly increased by 0.1% in CRESTOR-treated patients compared to placebo-treated patients. The number of patients with a HbA1c >6.5% at the end of the trial was significantly higher in CRESTOR-treated versus placebo-treated patients *[see Warnings and Precautions (5.5) and Clinical Studies (14)]*.

Adverse reactions reported in ≥2% of patients and at a rate greater than placebo are shown in Table 4.

Table 4: Adverse Reactions Reported in ≥2% of Patients Treated with CRESTOR and > Placebo in the JUPITER Trial

Adverse Reactions	Placebo N=8901 %	CRESTOR 20 mg N=8901 %
Myalgia	6.6	7.6
Arthralgia	3.2	3.8
Constipation	3.0	3.3
Diabetes mellitus	2.3	2.8
Nausea	2.3	2.4

Pediatric Patients with HeFH

In a 12-week controlled study in pediatric patients 10 to 17 years of age with HeFH with CRESTOR 5 to 20 mg daily *[see Use in Specific Populations (8.4) and Clinical Studies (14)]*, elevations in serum CK greater than 10 x ULN were observed more frequently in CRESTOR-treated patients compared with patients receiving placebo. Four of 130 (3%) patients treated with CRESTOR (2 treated with 10 mg and 2 treated with 20 mg) had increased CK greater than 10 x ULN, compared to 0 of 46 patients on placebo.

6.2 Postmarketing Experience

The following adverse reactions have been identified during postapproval use of CRESTOR. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Blood Disorders: thrombocytopenia

Hepatobiliary Disorders: hepatitis, jaundice, fatal and non-fatal hepatic failure

Musculoskeletal Disorders: arthralgia, rare reports of immune-mediated necrotizing myopathy associated with statin use

Nervous System Disorders: peripheral neuropathy, rare postmarketing reports of cognitive impairment (e.g., memory loss, forgetfulness, amnesia, memory impairment, and confusion)

associated with the use of all statins. The reports are generally nonserious, and reversible upon statin discontinuation, with variable times to symptom onset (1 day to years) and symptom resolution (median of 3 weeks).

Psychiatric Disorders: depression, sleep disorders (including insomnia and nightmares)

Reproductive System and Breast Disorders: gynecomastia

Respiratory Disorders: interstitial lung disease

Skin and Subcutaneous Tissue Disorders: drug reaction with eosinophilia and systemic symptoms (DRESS), lichenoid drug eruption

7 DRUG INTERACTIONS

7.1 Drug Interactions that Increase the Risk of Myopathy and Rhabdomyolysis with CRESTOR

Rosuvastatin is a substrate of CYP2C9 and transporters (such as OATP1B1, BCRP). Rosuvastatin plasma levels can be significantly increased with concomitant administration of inhibitors of CYP2C9 and transporters. Table 5 includes a list of drugs that increase the risk of myopathy and rhabdomyolysis when used concomitantly with CRESTOR and instructions for preventing or managing them *[see Warnings and Precautions (5.1) and Clinical Pharmacology (12.3)]*.

Table 5: Drug Interactions that Increase the Risk of Myopathy and Rhabdomyolysis with CRESTOR

Cyclosporine	
Clinical Impact:	Cyclosporine increased rosuvastatin exposure 7-fold. The risk of myopathy and rhabdomyolysis is increased with concomitant use of cyclosporine or gemfibrozil with CRESTOR.
Intervention:	If used concomitantly, do not exceed a dose of CRESTOR 5 mg once daily.
Teriflunomide	
Clinical Impact:	Teriflunomide increased rosuvastatin exposure more than 2.5-fold. The risk of myopathy and rhabdomyolysis is increased with concomitant use.
Intervention:	In patients taking teriflunomide, do not exceed a dose of CRESTOR 10 mg once daily.
Capmatinib	
Clinical Impact:	Capmatinib increased rosuvastatin exposure more than 2.1-fold. The risk of myopathy and rhabdomyolysis is increased with concomitant use.
Intervention:	In patients taking capmatinib, do not exceed a dose of CRESTOR 10 mg once daily.

Fostamatinib		
Clinical Impact:	Fostamatinib increased rosuvastatin exposure more than 2.0-fold. The risk of myopathy and rhabdomyolysis is increased with concomitant use.	
Intervention:	In patients taking fostamatinib, do not exceed a dose of CRESTOR 20 mg once daily.	
Febuxostat		
Clinical Impact:	Febuxostat increased rosuvastatin exposure more than 1.9-fold. The risk of myopathy and rhabdomyolysis is increased with concomitant use.	
Intervention:	In patients taking febuxostat, do not exceed a dose of CRESTOR 20 mg once daily.	
Gemfibrozil		
Clinical Impact:	Gemfibrozil significantly increased rosuvastatin exposure and gemfibrozil may cause myopathy when given alone. The risk of myopathy and rhabdomyolysis is increased with concomitant use of gemfibrozil with CRESTOR.	
Intervention:	Avoid concomitant use of gemfibrozil with CRESTOR. If used concomitantly, initiate CRESTOR at 5 mg once daily and do not exceed a dose of CRESTOR 10 mg once daily.	
Tafamidis		
Clinical Impact:	Tafamidis significantly increased rosuvastatin exposure and tafamidis may cause myopathy when given alone. The risk of myopathy and rhabdomyolysis is increased with concomitant use of tafamidis with CRESTOR.	
Intervention:	Avoid concomitant use of tafamidis with CRESTOR. If used concomitantly, initiate CRESTOR at 5 mg once daily and do not exceed a dose of CRESTOR 10 mg once daily. Monitor for signs of myopathy and rhabdomyolysis if used concomitantly with CRESTOR.	
Anti-Viral Medications		
Clinical Impact:	Rosuvastatin plasma levels were significantly increased with concomitant administration of many anti-viral drugs, which increases the risk of myopathy and rhabdomyolysis.	
Intervention:	• Sofosbuvir/velpatasvir/voxilaprevir • Ledipasvir/sofosbuvir	Avoid concomitant use with CRESTOR.
	• Simeprevir • Dasabuvir/ombitasvir/paritaprevir/ritonavir • Elbasvir/grazoprevir • Sofosbuvir/velpatasvir • Glecaprevir/pibrentasvir • Atazanavir/ritonavir • Lopinavir/ritonavir	Initiate with CRESTOR 5 mg once daily, and do not exceed a dose of CRESTOR 10 mg once daily.

Darolutamide	
Clinical Impact:	Darolutamide increased rosuvastatin exposure more than 5-fold. The risk of myopathy and rhabdomyolysis is increased with concomitant use.
Intervention:	In patients taking darolutamide, do not exceed a dose of CRESTOR 5 mg once daily.
Regorafenib	
Clinical Impact:	Regorafenib increased rosuvastatin exposure and may increase the risk of myopathy.
Intervention:	In patients taking regorafenib, do not exceed a dose of CRESTOR 10 mg once daily.
Fenofibrates (e.g., fenofibrate and fenofibric acid)	
Clinical Impact:	Fibrates may cause myopathy when given alone. The risk of myopathy and rhabdomyolysis is increased with concomitant use of fibrates with CRESTOR.
Intervention:	Consider if the benefit of using fibrates concomitantly with CRESTOR outweighs the increased risk of myopathy and rhabdomyolysis. If concomitant use is decided, monitor patients for signs and symptoms of myopathy, particularly during initiation of therapy and during upward dose titration of either drug.
Niacin	
Clinical Impact:	Cases of myopathy and rhabdomyolysis have occurred with concomitant use of lipid-modifying doses (≥1 g/day) of niacin with CRESTOR.
Intervention:	Consider if the benefit of using lipid-modifying doses (≥1 g/day) of niacin concomitantly with CRESTOR outweighs the increased risk of myopathy and rhabdomyolysis. If concomitant use is decided, monitor patients for signs and symptoms of myopathy, particularly during initiation of therapy and during upward dose titration of either drug.
Colchicine	
Clinical Impact:	Cases of myopathy and rhabdomyolysis have been reported with concomitant use of colchicine with CRESTOR.
Intervention:	Consider if the benefit of using colchicine concomitantly with CRESTOR outweighs the increased risk of myopathy and rhabdomyolysis. If concomitant use is decided, monitor patients for signs and symptoms of myopathy, particularly during initiation of therapy and during upward dose titration of either drug.

7.2 Drug Interactions that Decrease the Efficacy of CRESTOR

Table 6 presents drug interactions that may decrease the efficacy of CRESTOR and instructions for preventing or managing them.

Table 6: Drug Interactions that Decrease the Efficacy of CRESTOR

Antacids	
Clinical Impact:	Concomitant aluminum and magnesium hydroxide combination antacid administration decreased the mean exposure of rosuvastatin 50% *[see Clinical Pharmacology (12.3)]*.
Intervention:	In patients taking antacid, administer CRESTOR at least 2 hours after the antacid .

7.3 CRESTOR Effects on Other Drugs

Table 7 presents CRESTOR's effect on other drugs and instructions for preventing or managing them.

Table 7: CRESTOR Effects on Other Drugs

Warfarin	
Clinical Impact:	Rosuvastatin significantly increased the INR in patients receiving warfarin *[see Clinical Pharmacology (12.3)]*.
Intervention:	In patients taking warfarin, obtain an INR before starting CRESTOR and frequently enough after initiation, dose titration or discontinuation to ensure that no significant alteration in INR occurs. Once the INR is stable, monitor INR at regularly recommended intervals.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

Discontinue CRESTOR when pregnancy is recognized. Alternatively, consider the ongoing therapeutic needs of the individual patient.

CRESTOR decreases synthesis of cholesterol and possibly other biologically active substances derived from cholesterol; therefore, CRESTOR may cause fetal harm when administered to pregnant patients based on the mechanism of action *[see Clinical Pharmacology (12.1)]*. In addition, treatment of hyperlipidemia is not generally necessary during pregnancy. Atherosclerosis is a chronic process and the discontinuation of lipid-lowering drugs during pregnancy should have little impact on the outcome of long-term therapy of primary hyperlipidemia for most patients.

Available data from case series and prospective and retrospective observational cohort studies over decades of use with statins in pregnant women have not identified a drug-associated risk of major congenital malformations. Published data from prospective and retrospective observational

cohort studies with CRESTOR use in pregnant women are insufficient to determine if there is a drug-associated risk of miscarriage *(see Data)*.

In animal reproduction studies, no adverse developmental effects were observed in pregnant rats or rabbits orally administered rosuvastatin during the period of organogenesis at doses that resulted in systemic exposures equivalent to human exposures at the maximum recommended human dose (MRHD) of 40 mg/day, based on AUC and body surface area (mg/m^2), respectively *(see Data)*.

The estimated background risk of major birth defects and miscarriage for the indicated population is unknown. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2 to 4% and 15 to 20%, respectively.

Data

Human Data

A Medicaid cohort linkage study of 1152 statin-exposed pregnant women compared to 886,996 controls did not find a significant teratogenic effect from maternal use of statins in the first trimester of pregnancy, after adjusting for potential confounders – including maternal age, diabetes mellitus, hypertension, obesity, and alcohol and tobacco use – using propensity score-based methods. The relative risk of congenital malformations between the group with statin use and the group with no statin use in the first trimester was 1.07 (95% confidence interval 0.85 to 1.37) after controlling for confounders, particularly pre-existing diabetes mellitus. There were also no statistically significant increases in any of the organ-specific malformations assessed after accounting for confounders. In the majority of pregnancies, statin treatment was initiated prior to pregnancy and was discontinued at some point in the first trimester when pregnancy was identified. Study limitations include reliance on physician coding to define the presence of a malformation, lack of control for certain confounders such as body mass index, use of prescription dispensing as verification for the use of a statin, and lack of information on non-live births.

Animal Data

In female rats given 5, 15 and 50 mg/kg/day before mating and continuing through to gestation day 7 resulted in decreased fetal body weight (female pups) and delayed ossification at 50 mg/kg/day (10 times the human exposure at the MRHD dose of 40 mg/day based on AUC).

In pregnant rats given 2, 10 and 50 mg/kg/day of rosuvastatin from gestation day 7 through lactation day 21 (weaning), decreased pup survival occurred at 50 mg/kg/day (dose equivalent to 12 times the MRHD of 40 mg/day based body surface area).

In pregnant rabbits given 0.3, 1, and 3 mg/kg/day of rosuvastatin from gestation day 6 to day 18, decreased fetal viability and maternal mortality was observed at 3 mg/kg/day (dose equivalent to the MRHD of 40 mg/day based on body surface area).

Rosuvastatin crosses the placenta in rats and rabbits and is found in fetal tissue and amniotic fluid at 3% and 20%, respectively, of the maternal plasma concentration following a single 25 mg/kg oral gavage dose on gestation day 16 in rats. In rabbits, fetal tissue distribution was 25% of maternal plasma concentration after a single oral gavage dose of 1 mg/kg on gestation day 18.

8.2 Lactation

Risk Summary

Limited data from case reports in published literature indicate that CRESTOR is present in human milk. There is no available information on the effects of the drug on the breastfed infant or the effects of the drug on milk production. Statins, including CRESTOR, decrease cholesterol synthesis and possibly the synthesis of other biologically active substances derived from cholesterol and may cause harm to the breastfed infant.

Because of the potential for serious adverse reactions in a breastfed infant, based on the mechanism of action, advise patients that breastfeeding is not recommended during treatment with CRESTOR *[see Use in Specific Populations (8.1) and Clinical Pharmacology (12.1)]*.

8.4 Pediatric Use

The safety and effectiveness of CRESTOR as an adjunct to diet to reduce LDL-C have been established in pediatric patients 8 years of age and older with HeFH. Use of CRESTOR for this indication is based on one 12-week controlled trial with a 40-week open-label extension period in 176 pediatric patients 10 years of age and older with HeFH and one 2-year open-label, uncontrolled trial in 175 pediatric patients 8 years of age and older with HeFH *[*see *Clinical Studies (14)]*. In the 1-year trial with a 12-week controlled phase, there was no detectable effect of CRESTOR on growth, weight, BMI (body mass index), or sexual maturation in patients aged 10 to 17 years.

The safety and effectiveness of CRESTOR as an adjunct to other LDL-C-lowering therapies to reduce LDL-C have been established pediatric patients 7 years of age and older with HoFH. Use of CRESTOR for this indication is based on a randomized, placebo-controlled, cross-over study in 14 pediatric patients 7 years of age and older with HoFH *[*see *Clinical Studies (14)]*.

The safety and effectiveness of CRESTOR have not been established in pediatric patients younger than 8 years of age with HeFH, younger than 7 years of age with HoFH, or in pediatric patients with other types of hyperlipidemia (other than HeFH or HoFH).

8.5 Geriatric Use

Of the total number of CRESTOR-treated patients in clinical studies, 3159 (31%) were 65 years and older, and 698 (6.8%) were 75 years and older. No overall differences in safety or effectiveness were observed between these subjects and younger subjects.

Advanced age (≥65 years) is a risk factor for CRESTOR-associated myopathy and rhabdomyolysis. Dose selection for an elderly patient should be cautious, recognizing the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy and the higher risk of myopathy. Monitor geriatric patients receiving CRESTOR for the increased risk of myopathy *[see Warnings and Precautions (5.1)]*.

8.6 Renal Impairment

Rosuvastatin exposure is not influenced by mild to moderate renal impairment (CL_{cr} ≥30 mL/min/1.73 m^2). Exposure to rosuvastatin is increased to a clinically significant extent in patients with severe renal impairment (CL_{cr} <30 mL/min/1.73 m^2) who are not receiving hemodialysis *[see Clinical Pharmacology (12.3)]*.

Renal impairment is a risk factor for myopathy and rhabdomyolysis. Monitor all patients with renal impairment for development of myopathy. In patients with severe renal impairment not on hemodialysis, the recommended starting dosage is 5 mg daily and should not exceed 10 mg daily *[see Dosage and Administration (2.5) and Warnings and Precautions (5.1)]*.

8.7 Hepatic Impairment

CRESTOR is contraindicated in patients with acute liver failure or decompensated cirrhosis. Chronic alcohol liver disease is known to increase rosuvastatin exposure. Patients who consume substantial quantities of alcohol and/or have a history of liver disease may be at increased risk for hepatic injury *[see Contraindications (4), Warning and Precautions (5.3) and Clinical Pharmacology (12.3)]*.

8.8 Asian Patients

Pharmacokinetic studies have demonstrated an approximate 2-fold increase in median exposure to rosuvastatin in Asian subjects when compared with White controls. Adjust the CRESTOR dosage in Asian patients *[see Dosage and Administration (2.4) and Clinical Pharmacology (12.3)]*.

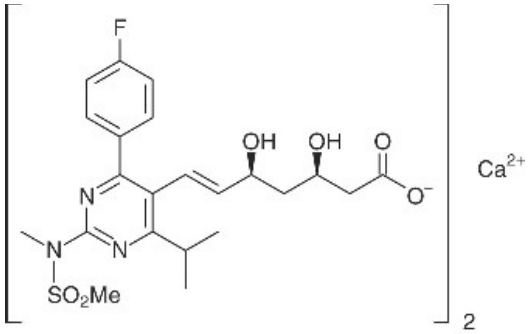
10 OVERDOSAGE

No specific antidotes for CRESTOR are known. Hemodialysis does not significantly enhance clearance of rosuvastatin. Contact Poison Control (1-800-222-1222) for latest recommendations.

11 DESCRIPTION

CRESTOR (rosuvastatin) is a 3-hydroxy-3-methylglutaryl coenzyme A (HMG CoA)-reductase inhibitor.

The chemical name for rosuvastatin calcium is bis[(E)-7-[4-(4-fluorophenyl)-6-isopropyl-2-[methyl(methylsulfonyl)amino] pyrimidin-5-yl](3R,5S)-3,5-dihydroxyhept-6-enoic acid] calcium salt with the following structural formula:



The empirical formula for rosuvastatin calcium is $(C_{22}H_{27}FN_3O_6S)_2Ca$ and the molecular weight is 1001.14. Rosuvastatin calcium is a white amorphous powder that is sparingly soluble in water and methanol, and slightly soluble in ethanol. Rosuvastatin calcium is a hydrophilic compound with a partition coefficient (octanol/water) of 0.13 at pH of 7.0.

CRESTOR tablets for oral use contain rosuvastatin 5 mg, 10 mg, 20 mg, or 40 mg (equivalent to 5.2 mg, 10.4 mg, 20.8 mg, and 41.6 mg rosuvastatin calcium) and the following inactive ingredients: crospovidone NF, hypromellose NF, lactose monohydrate NF, magnesium stearate NF, microcrystalline cellulose NF, red ferric oxide NF, titanium dioxide USP, triacetin NF, tribasic calcium phosphate NF and yellow ferric oxide.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

CRESTOR is an inhibitor of HMG-CoA reductase, the rate-limiting enzyme that converts 3-hydroxy-3-methylglutaryl coenzyme A to mevalonate, a precursor of cholesterol.

12.2 Pharmacodynamics

Inhibition of HMG-CoA reductase by rosuvastatin accelerates the expression of LDL-receptors, followed by the uptake of LDL-C from blood to the liver, leading to a decrease in plasma LDL-C and total cholesterol. Sustained inhibition of cholesterol synthesis in the liver also decreases levels of very-low-density lipoproteins. The maximum LDL-C reduction of CRESTOR is usually achieved by 4 weeks and is maintained after that.

12.3 Pharmacokinetics

Absorption

In clinical pharmacology studies in man, peak plasma concentrations of rosuvastatin were reached 3 to 5 hours following oral dosing. Both C_{max} and AUC increased in approximate proportion to CRESTOR dose. The absolute bioavailability of rosuvastatin is approximately

20%. The AUC of rosuvastatin does not differ following evening or morning drug administration.

Effect of food

Administration of CRESTOR with food did not affect the AUC of rosuvastatin.

Distribution

Mean volume of distribution at steady-state of rosuvastatin is approximately 134 liters. Rosuvastatin is 88% bound to plasma proteins, mostly albumin. This binding is reversible and independent of plasma concentrations.

Elimination

Metabolism

Rosuvastatin is not extensively metabolized; approximately 10% of a radiolabeled dose is recovered as metabolite. The major metabolite is N-desmethyl rosuvastatin, which is formed principally by cytochrome P450 \ 2C9, and *in vitro* studies have demonstrated that N-desmethyl rosuvastatin has approximately one-sixth to one-half the HMG-CoA reductase inhibitory activity of the parent compound. Overall, greater than 90% of active plasma HMG-CoA reductase inhibitory activity is accounted for by the parent compound.

Excretion

Following oral administration, rosuvastatin and its metabolites are primarily excreted in the feces (90%). After an intravenous dose, approximately 28% of total body clearance was via the renal route, and 72% by the hepatic route. The elimination half-life of rosuvastatin is approximately 19 hours.

Specific Populations

Geriatric Patients

There were no differences in plasma concentrations of rosuvastatin between the nonelderly and elderly populations (age ≥65 years).

Pediatric Patients

In a population pharmacokinetic analysis of two pediatric trials involving patients with heterozygous familial hypercholesterolemia 10 to 17 years of age and 8 to 17 years of age, respectively, rosuvastatin exposure appeared comparable to or lower than rosuvastatin exposure in adult patients.

Male and Female Patients

There were no differences in plasma concentrations of rosuvastatin between men and women.

Racial or Ethnic Groups

A population pharmacokinetic analysis revealed no clinically relevant differences in pharmacokinetics among Caucasian, Hispanic, and Black or Afro-Caribbean groups. However, pharmacokinetic studies, including one conducted in the US, have demonstrated an approximate 2-fold elevation in median exposure (AUC and C_{max}) in Asian subjects when compared with a Caucasian control group.

Patients with Renal Impairment

Mild to moderate renal impairment (CL_{cr} ≥30 mL/min/1.73 m^2) had no influence on plasma concentrations of rosuvastatin. However, plasma concentrations of rosuvastatin increased to a clinically significant extent (about 3-fold) in patients with severe renal impairment (CL_{cr} <30 mL/min/1.73 m^2) not receiving hemodialysis compared with healthy subjects (CL_{cr} >80 mL/min/1.73 m^2).

Steady-state plasma concentrations of rosuvastatin in patients on chronic hemodialysis were approximately 50% greater compared with healthy volunteer subjects with normal renal function.

Patients with Hepatic Impairment

In patients with chronic alcohol liver disease, plasma concentrations of rosuvastatin were modestly increased.

In patients with Child-Pugh A disease, C_{max} and AUC were increased by 60% and 5%, respectively, as compared with patients with normal liver function. In patients with Child-Pugh B disease, C_{max} and AUC were increased 100% and 21%, respectively, compared with patients with normal liver function.

Drug Interactions Studies

Rosuvastatin clearance is not dependent on metabolism by cytochrome P450 3A4 to a clinically significant extent.

Rosuvastatin is a substrate for certain transporter proteins including the hepatic uptake transporter organic anion-transporting polyprotein 1B1 (OATP1B1) and efflux transporter breast cancer resistance protein (BCRP). Concomitant administration of CRESTOR with medications that are inhibitors of these transporter proteins (e.g. cyclosporine, certain HIV protease inhibitors) may result in increased rosuvastatin plasma concentrations *[see Dosage and Administration (2.6) and Drug Interactions (7.1)]*.

Table 8: Effect of Coadministered Drugs on Rosuvastatin Systemic Exposure

Coadministered drug and dosing regimen	**Rosuvastatin**		
		Mean Ratio (ratio with/without coadministered drug) No Effect=1.0	
	Dose (mg)[1]	**Change in AUC**	**Change in C_{max}**
Sofosbuvir/velpatasvir/voxilaprevir (400 mg-100 mg-100 mg) + Voxilaprevir (100 mg) once daily for 15 days	10 mg, single dose	7.39[2] (6.68-8.18)[3]	18.88[2] (16.23-21.96)[3]
Cyclosporine – stable dose required (75 mg – 200 mg BID)	10 mg, QD for 10 days	7.1[2]	11[2]
Darolutamide 600 mg BID, 5 days	5 mg, single dose	5.2[2]	~5[2]
Regorafenib 160 mg OD, 14 days	5 mg, single dose	3.8[2]	4.6[2]
Atazanavir/ritonavir combination 300 mg/100 mg QD for 8 days	10 mg	3.1[2]	7[2]
Simeprevir 150 mg QD, 7 days	10 mg, single dose	2.8[2] (2.3-3.4)[3]	3.2[2] (2.6-3.9)[3]
Velpatasvir 100 mg once daily	10 mg, single dose	2.69[2] (2.46-2.94)[3]	2.61[2] (2.32-2.92)[3]
Ombitasvir 25 mg/paritaprevir 150 mg/ ritonavir 100 mg + dasabuvir 400 mg BID	5 mg, single dose	2.59[2] (2.09-3.21)[3]	7.13[2] (5.11-9.96)[3]
Teriflunomide	Not available	2.51[2]	2.65[2]
Elbasvir 50 mg/grazoprevir 200 mg once daily	10 mg, single dose	2.26[2] (1.89-2.69)[3]	5.49[2] (4.29-7.04)[3]
Glecaprevir 400 mg/pibrentasvir 120 mg once daily	5 mg, once daily	2.15[2] (1.88-2.46)[3]	5.62[2] (4.80-6.59)[3]
Lopinavir/ritonavir combination 400 mg/100 mg BID for 17 days	20 mg, QD for 7 days	2.1[2] (1.7-2.6)[3]	5[2] (3.4-6.4)[3]
Capmatinib 400 mg BID	10 mg, single dose	2.08[2] (1.56-2.76)[3]	3.04[2] (2.36-3.92)[3]
Fostamatinib 100 mg BID	20 mg, single dose	1.96[2] (1.77-2.15)[3]	1.88[2] (1.69-2.09)[3]
Febuxostat 120 mg OD for 4 days	10 mg, single dose	1.9[2] (1.5-2.5)[3]	2.1[2] (1.8-2.6)[3]
Gemfibrozil 600 mg BID for 7 days	80 mg	1.9[2]	2.2[2]

Table 8: Effect of Coadministered Drugs on Rosuvastatin Systemic Exposure

Coadministered drug and dosing regimen	**Rosuvastatin**		
		Mean Ratio (ratio with/without coadministered drug) No Effect=1.0	
	Dose (mg)[1]	**Change in AUC**	**Change in C_{max}**
		(1.6-2.2)[3]	(1.8-2.7)[3]
Tafamidis 61 mg QD, 7 days	10 mg	1.97[2] (1.68-2.31)[3]	1.86[2] (1.59-2.16)[3]
Eltrombopag 75 mg QD, 5 days	10 mg	1.6 (1.4-1.7)[3]	2 (1.8-2.3)[3]
Darunavir 600 mg/ritonavir 100 mg BID, 7 days	10 mg, QD for 7 days	1.5 (1.0-2.1)[3]	2.4 (1.6-3.6)[3]
Tipranavir/ritonavir combination 500 mg/200 mg BID for 11 days	10 mg	1.4 (1.2-1.6)[3]	2.2 (1.8-2.7)[3]
Dronedarone 400 mg BID	10 mg	1.4	
Itraconazole 200 mg QD, 5 days	10 mg or 80 mg	1.4 (1.2-1.6)[3] 1.3 (1.1-1.4)[3]	1.4 (1.2-1.5)[3] 1.2 (0.9-1.4)[3]
Ezetimibe 10 mg QD, 14 days	10 mg, QD for 14 days	1.2 (0.9-1.6)[3]	1.2 (0.8-1.6)[3]
Fosamprenavir/ritonavir 700 mg/100 mg BID for 7 days	10 mg	1.1	1.5
Fenofibrate 67 mg TID for 7 days	10 mg	↔	1.2 (1.1-1.3)[3]
Rifampicin 450 mg QD, 7 days	20 mg	↔	
Aluminum & magnesium hydroxide combination antacid Administered simultaneously Administered 2 hours apart	40 mg 40 mg	0.5[2] (0.4-0.5)[3] 0.8 (0.7-0.9)[3]	0.5[2] (0.4-0.6)[3] 0.8 (0.7-1.0)[3]
Ketoconazole 200 mg BID for 7 days	80 mg	1.0 (0.8-1.2)[3]	1.0 (0.7-1.3)[3]
Fluconazole 200 mg QD for 11 days	80 mg	1.1 (1.0-1.3)[3]	1.1 (0.9-1.4)[3]
Erythromycin 500 mg QID for 7 days	80 mg	0.8 (0.7-0.9)[3]	0.7 (0.5-0.9)[3]

QD= Once daily, BID= Twice daily, TID= Three times daily, QID= Four times daily

[1] Single dose unless otherwise noted.

[2] Clinically significant *[see Dosage and Administration (2) and Warnings and Precautions (5)]*
[3] Mean ratio with 90% CI (with/without coadministered drug, e.g., 1= no change, 0.7 = 30% decrease, 11=11-fold increase in exposure)

Table 9: Effect of Rosuvastatin Coadministration on Systemic Exposure to Other Drugs

Rosuvastatin Dosage Regimen	**Coadministered Drug**		
		Mean Ratio (ratio with/without coadministered drug) No Effect=1.0	
	Name and Dose	**Change in AUC**	**Change in C_{max}**
40 mg QD for 10 days	Warfarin[1] 25 mg single dose	R- Warfarin 1.0 (1.0-1.1)[2] S-Warfarin 1.1 (1.0-1.1)[2]	R-Warfarin 1.0 (0.9-1.0)[2] S-Warfarin 1.0 (0.9-1.1)[2]
40 mg QD for 12 days	Digoxin 0.5 mg single dose	1.0 (0.9-1.2)[2]	1.0 (0.9-1.2)[2]
40 mg QD for 28 days	Oral Contraceptive (ethinyl estradiol 0.035 mg & norgestrel 0.180, 0.215 and 0.250 mg) QD for 21 Days	EE 1.3 (1.2-1.3)[2] NG 1.3 (1.3-1.4)[2]	EE 1.3 (1.2-1.3)[2] NG 1.2 (1.1-1.3)[2]

EE = ethinyl estradiol, NG = norgestrel, QD= Once daily
[1] Clinically significant pharmacodynamic effects *[see Drug Interactions (7.3)]*
[2] Mean ratio with 90% CI (with/without coadministered drug, e.g., 1= no change, 0.7=30% decrease, 11=11-fold increase in exposure)

12.5 Pharmacogenomics

Disposition of rosuvastatin, involves OATP1B1 and other transporter proteins. Higher plasma concentrations of rosuvastatin have been reported in very small groups of patients (n=3 to 5) who have two reduced function alleles of the gene that encodes OATP1B1 (*SLCO1B1* 521T > C). The frequency of this genotype (i.e., *SLCO1B1* 521 C/C) is generally lower than 5% in most racial/ethnic groups. The impact of this polymorphism on efficacy and/or safety of CRESTOR has not been clearly established.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

In a 104-week carcinogenicity study in rats at dose levels of 2, 20, 60, or 80 mg/kg/day by oral gavage, the incidence of uterine stromal polyps was significantly increased in females at

80 mg/kg/day at systemic exposure 20 times the human exposure at 40 mg/day based on AUC. Increased incidence of polyps was not seen at lower doses.

In a 107-week carcinogenicity study in mice given 10, 60, or 200 mg/kg/day by oral gavage, an increased incidence of hepatocellular adenoma/carcinoma was observed at 200 mg/kg/day at systemic exposures 20 times the human exposure at 40 mg/day based on AUC. An increased incidence of hepatocellular tumors was not seen at lower doses.

Rosuvastatin was not mutagenic or clastogenic with or without metabolic activation in the Ames test with *Salmonella typhimurium* and *Escherichia coli*, the mouse lymphoma assay, and the chromosomal aberration assay in Chinese hamster lung cells. Rosuvastatin was negative in the *in vivo* mouse micronucleus test.

In rat fertility studies with oral gavage doses of 5, 15, 50 mg/kg/day, males were treated for 9 weeks prior to and throughout mating and females were treated 2 weeks prior to mating and throughout mating until gestation day 7. No adverse effect on fertility was observed at 50 mg/kg/day (systemic exposures up to 10 times the human exposure at 40 mg/day based on AUC). In testicles of dogs treated with rosuvastatin at 30 mg/kg/day for one month, spermatidic giant cells were seen. Spermatidic giant cells were observed in monkeys after 6-month treatment at 30 mg/kg/day in addition to vacuolation of seminiferous tubular epithelium. Exposures in the dog were 20 times and in the monkey 10 times the human exposure at 40 mg/day based on body surface area. Similar findings have been seen with other drugs in this class.

14 CLINICAL STUDIES

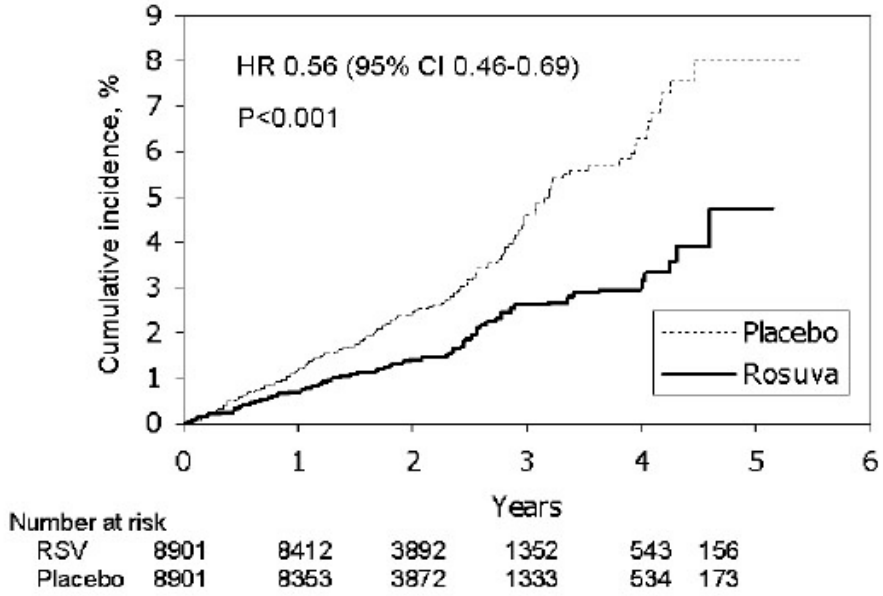
Primary Prevention of Cardiovascular Disease

In the Justification for the Use of Statins in Primary Prevention: An Intervention Trial Evaluating Rosuvastatin (JUPITER) study, the effect of CRESTOR on the occurrence of major cardiovascular (CV) disease events was assessed in 17,802 men (≥50 years) and women (≥60 years) who had no clinically evident cardiovascular disease, LDL-C levels <130 mg/dL and hsCRP levels ≥2 mg/L. The study population had an estimated baseline coronary heart disease risk of 11.6% over 10 years based on the Framingham risk criteria and included a high percentage of patients with additional risk factors such as hypertension (58%), low HDL-C levels (23%), cigarette smoking (16%), or a family history of premature CHD (12%). Patients had a median baseline LDL-C of 108 mg/dL and hsCRP of 4.3 mg/L. Patients were randomly assigned to placebo (n=8901) or CRESTOR 20 mg once daily (n=8901) and were followed for a mean duration of 2 years. The JUPITER study was stopped early by the Data Safety Monitoring Board due to meeting predefined stopping rules for efficacy in CRESTOR-treated subjects.

The primary end point was a composite end point consisting of the time-to-first occurrence of any of the following major CV events: CV death, nonfatal myocardial infarction, nonfatal stroke, hospitalization for unstable angina or an arterial revascularization procedure.

CRESTOR significantly reduced the risk of major CV events (252 events in the placebo group vs. 142 events in the rosuvastatin group) with a statistically significant ($p<0.001$) relative risk reduction of 44% and absolute risk reduction of 1.2% (see Figure 1). The risk reduction for the primary end point was consistent across the following predefined subgroups: age, sex, race, smoking status, family history of premature CHD, body mass index, LDL-C, HDL-C, and hsCRP levels.

Figure 1. Time to First Occurrence of Major Cardiovascular Events in JUPITER

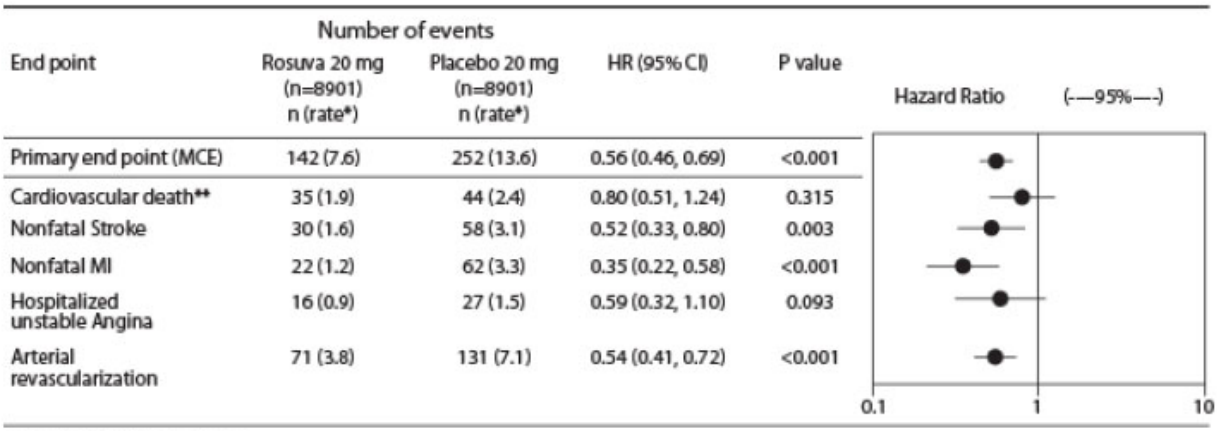


The individual components of the primary end point are presented in Figure 3. CRESTOR significantly reduced the risk of nonfatal myocardial infarction, nonfatal stroke, and arterial revascularization procedures. There were no significant treatment differences between the CRESTOR and placebo groups for death due to cardiovascular causes or hospitalizations for unstable angina.

CRESTOR significantly reduced the risk of myocardial infarction (6 fatal events and 62 nonfatal events in placebo-treated subjects vs. 9 fatal events and 22 nonfatal events in CRESTOR-treated subjects) and the risk of stroke (6 fatal events and 58 nonfatal events in placebo-treated subjects vs. 3 fatal events and 30 nonfatal events in CRESTOR-treated subjects).

In a post-hoc subgroup analysis of JUPITER subjects (rosuvastatin=725, placebo=680) with a hsCRP ≥2 mg/L and no other traditional risk factors (smoking, BP ≥140/90 or taking antihypertensives, low HDL-C) other than age, after adjustment for high HDL-C, there was no significant treatment benefit with CRESTOR treatment.

Figure 2. Major CV Events by Treatment Group in JUPITER



* event rate/1000-patient years
** Cardiovascular death included fatal MI, fatal stroke, sudden death, and other adjudicated causes of CV death

At one year, CRESTOR increased HDL-C and reduced LDL-C, hsCRP, total cholesterol and serum triglyceride levels ($p<0.001$ for all versus placebo).

Primary Hyperlipidemia in Adults

CRESTOR reduces Total-C, LDL-C, ApoB, non-HDL-C, and TG, and increases HDL-C, in adult patients with hyperlipidemia and mixed dyslipidemia.

In a multicenter, double-blind, placebo-controlled study in patients with hyperlipidemia, CRESTOR given as a single daily dose (5 to 40 mg) for 6 weeks significantly reduced Total-C, LDL-C, non-HDL-C, and ApoB, across the dose range (Table 10).

Table 10: Lipid-modifying Effect of CRESTOR in Adult Patients with Hyperlipidemia (Adjusted Mean % Change from Baseline at Week 6)

Dose	N	Total-C	LDL-C	Non-HDL-C	ApoB	TG	HDL-C
Placebo	13	-5	-7	-7	-3	-3	3
CRESTOR 5 mg	17	-33	-45	-44	-38	-35	13
CRESTOR 10 mg	17	-36	-52	-48	-42	-10	14
CRESTOR 20 mg	17	-40	-55	-51	-46	-23	8
CRESTOR 40 mg	18	-46	-63	-60	-54	-28	10

CRESTOR was compared with the statins (atorvastatin, simvastatin, and pravastatin) in a multicenter, open-label, dose-ranging study of 2240 patients with hyperlipidemia or mixed dyslipidemia. After randomization, patients were treated for 6 weeks with a single daily dose of either CRESTOR, atorvastatin, simvastatin, or pravastatin (Figure 3 and Table 11).

16 HOW SUPPLIED/STORAGE AND HANDLING

CRESTOR tablets are supplied as:

Strength	How Supplied	NDC	Tablet Description
5 mg	bottles of 90 tablets	0310-7560-90	Yellow, round, biconvex, coated tablets. Debossed “ZD4522” and “5” on one side
10 mg	bottles of 90 tablets	0310-7570-90	Pink, round, biconvex, coated tablets. Debossed “ZD4522” and “10” on one side
20 mg	bottles of 90 tablets	0310-7580-90	Pink, round, biconvex, coated tablets. Debossed “ZD4522” and “20” on one side
40 mg	bottles of 30 tablets	0310-7590-30	Pink, oval, biconvex, coated tablets. Debossed “ZD4522” on one side and “40” on the other side

Storage

Store at controlled room temperature, 20ºC to 25ºC (68ºF to 77ºF); excursions permitted between 15°C and 30°C (59°F and 86°F) [see USP Controlled Room Temperature]. Protect from moisture.

17 PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Patient Information).

Myopathy and Rhabdomyolysis

Advise patients that CRESTOR may cause myopathy and rhabdomyolysis. Inform patients that the risk is also increased when taking certain types of medication and they should discuss all medication, both prescription and over the counter, with their healthcare provider. Instruct patients to promptly report any unexplained muscle pain, tenderness or weakness particularly if accompanied by malaise or fever *[see Warnings and Precautions (5.1), and Drug Interactions (7.1)]*.

Hepatic Dysfunction

Inform patients that CRESTOR may cause liver enzyme elevations and possibly liver failure. Advise patients to promptly report fatigue, anorexia, right upper abdominal discomfort, dark urine or jaundice *[see Warnings and Precautions (5.3)]*.

Increases in HbA1c and Fasting Serum Glucose Levels

Inform patients that increases in HbA1c and fasting serum glucose levels may occur with CRESTOR. Encourage patients to optimize lifestyle measures, including regular exercise, maintaining a healthy body weight, and making healthy food choices *[see Warnings and Precautions (5.5)]*.

Pregnancy

Advise pregnant patients and patients who can become pregnant of the potential risk to a fetus. Advise patients to inform their healthcare provider of a known or suspected pregnancy to discuss if CRESTOR should be discontinued *[see Use in Specific Populations (8.1)]*.

Lactation

Advise patients that breastfeeding during treatment with CRESTOR is not recommended *[see Use in Specific Populations (8.2)]*.

Concomitant Use of Antacids

When taking CRESTOR with an aluminum and magnesium hydroxide combination antacid, the antacid should be taken at least 2 hours after CRESTOR administration.

Missed Doses

If a dose is missed, advise patients not take an extra dose. Just resume the usual schedule.

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PATIENT INFORMATION

CRESTOR® (Kres-tor)

rosuvastatin

Tablets

Read this Patient Information carefully before you start taking CRESTOR and each time you get a refill. If you have any questions about CRESTOR, ask your doctor. Only your doctor can determine if CRESTOR is right for you.

What is CRESTOR?

CRESTOR is a prescription medicine that contains a cholesterol-lowering medicine called rosuvastatin.

- CRESTOR is used to:
  - reduce the risk of stroke, heart attack, and the need for procedures to improve blood flow to the heart called arterial revascularization in adults who do not have known heart disease but do have certain additional risk factors.
- CRESTOR is used along with diet to:
  - lower the level of low-density lipoprotein (LDL) cholesterol or "bad" cholesterol in adults with primary hyperlipidemia.
  - slow the buildup of fatty deposits (plaque) in the walls of blood vessels.
  - treat adults and children 8 years of age and older with high blood cholesterol due to heterozygous familial hypercholesterolemia (an inherited condition that causes high levels of LDL).
  - along with other cholesterol lowering treatments or alone if such treatments are unavailable in adults and children 7 years of age and older with homozygous familial hypercholesterolemia (an inherited condition that causes high levels of LDL).
  - treat adults with a type of high cholesterol called primary dysbetalipoproteinemia (type III hyperlipoproteinemia).
  - lower the level of fat in your blood (triglycerides) in adults with hypertriglyceridemia.

The safety and effectiveness of CRESTOR has not been established in children younger than 8 years of age with heterozygous familial hypercholesterolemia or children younger than 7 years of age with homozygous familial hypercholesterolemia or in children with other types of hyperlipidemias (other than HeFH or HoFH).

Who should not take CRESTOR?

Do not take CRESTOR if you:

- have liver problems.
- are allergic to rosuvastatin or any of the ingredients in CRESTOR. See the end of this leaflet for a complete list of ingredients in CRESTOR. Symptoms of allergic reactions include rash, itching, hives, and swelling.

What should I tell my doctor before and while taking CRESTOR?

Tell your doctor if you:

- have unexplained muscle aches or weakness.
- have or have had kidney problems.
- have or have had liver problems.
- drink more than 2 glasses of alcohol daily.
- have thyroid problems.
- are 65 years of age or older.
- are of Asian descent.
- are pregnant or think you may be pregnant, or are planning to become pregnant. If you become pregnant while taking CRESTOR, call your healthcare provider right away to discuss your CRESTOR treatment.
- are breastfeeding. CRESTOR can pass into your breast milk. Breastfeeding is not recommended while taking CRESTOR.

Tell your doctor about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

Taking CRESTOR with certain other medicines may affect each other causing side effects. CRESTOR may affect the way other medicines work, and other medicines may affect how CRESTOR works.

Especially tell your doctor if you take:

- cyclosporine (a medicine for your immune system)
- gemfibrozil (a fibric acid medicine for lowering cholesterol)

- fostamatinib (a medicine used to treat low platelet counts)
- febuxostat (a medicine used to treat and prevent high blood levels of uric acid)
- teriflunomide (a medicine used to treat relapsing remitting multiple sclerosis)
- capmatinib (a medicine for the treatment of non-small cell lung cancer)
- tafamidis (used to treat cardiomyopathy [enlarged and thickened heart muscle])
- darolutamide (a medicine for the treatment of prostate cancer)
- regorafenib (a medicine used to treat cancer of the colon and rectum)
- anti-viral medicines including certain HIV or hepatitis C virus drugs such as:
    - lopinavir, ritonavir, fosamprenavir, tipranavir, atazanavir, simeprevir
    - combination of
        - sofosbuvir/velpatasvir/voxilaprevir
        - dasabuvir/ombitasvir/paritaprevir/ritonavir
        - elbasvir/grazoprevir
        - sofosbuvir/velpatasvir
        - glecaprevir/pibrentasvir **and**
    - all other combinations with ledipasvir including ledipasvir/sofosbuvir
- certain anti-fungal medicines (such as itraconazole, ketoconazole and fluconazole)
- coumarin anticoagulants (medicines that prevent blood clots, such as warfarin)
- niacin or nicotinic acid
- fibric acid derivatives (such as fenofibrate)
- colchicine (a medicine used to treat gout)

Ask your doctor or pharmacist for a list of these medicines if you are not sure. Know the medicines you take. Keep a list of them to show your doctor and pharmacist when you get new medicine.

How should I take CRESTOR?

- Take CRESTOR exactly as your doctor tells you to take it.
- Take CRESTOR, by mouth, 1 time each day. Swallow the tablet whole.
- CRESTOR can be taken at any time of day, with or without food.
- **Do not** change your dose or stop CRESTOR without talking to your doctor, even if you are feeling well.
- Your doctor may do blood tests to check your cholesterol levels before and during your treatment with CRESTOR. Your doctor may change your dose of CRESTOR if needed.
- Your doctor may start you on a cholesterol lowering diet before giving you CRESTOR. Stay on this diet when you take CRESTOR.
- Wait at least 2 hours after taking CRESTOR to take an antacid that contains a combination of aluminum and magnesium hydroxide.
- If you miss a dose of CRESTOR, take your next dose at your normal scheduled time. **Do not take** an extra dose of CRESTOR**.**
- If you take too much CRESTOR or overdose, call your doctor or go to the nearest hospital emergency room right away.

What are the possible side effects of CRESTOR?

CRESTOR may cause serious side effects, including:

- **Muscle pain, tenderness and weakness (myopathy).** Muscle problems, including muscle breakdown, can be serious in some people and rarely cause kidney damage that can lead to death. Tell your doctor right away if:
    - you have unexplained muscle pain, tenderness, or weakness, especially if you have a fever or feel more tired than usual, while you take CRESTOR.
    - you have muscle problems that do not go away even after your doctor has told you to stop taking CRESTOR. Your doctor may do further tests to diagnose the cause of your muscle problems.

Your chances of getting muscle problems are higher if you:

- are taking certain other medicines while you take CRESTOR
- are 65 years of age or older
- have thyroid problems (hypothyroidism) that are not controlled
- have kidney problems

- are taking higher doses of CRESTOR

- **Liver problems.** Your doctor should do blood tests to check your liver before you start taking CRESTOR and if you have symptoms of liver problems while you take CRESTOR. Call your doctor right away if you have any of the following symptoms of liver problems:
  - feel unusually tired or weak
  - loss of appetite
  - upper belly pain
  - dark urine
  - yellowing of your skin or the whites of your eyes
- **Protein and blood in the urine.** CRESTOR may cause you to have protein and blood in your urine. If you develop protein or blood in your urine, your doctor may decrease your dose of CRESTOR.
- **Increase in blood sugar (glucose) levels**. CRESTOR may cause an increase in your blood sugar levels.

The most common side effects may include headache, muscle aches and pains, abdominal pain, weakness, and nausea.

Tell your doctor if you have any side effect that bothers you or that does not go away.

For more information, ask your doctor or pharmacist.
Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How should I store CRESTOR?

- Store CRESTOR at room temperature, between 68°F to 77°F (20°C to 25°C) and in a dry place.
- Safely throw away medicine that is out of date or no longer needed.

Keep CRESTOR and all medicines out of the reach of children.

General Information about the safe and effective use of CRESTOR

Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. Do not use CRESTOR for a condition for which it was not prescribed. Do not give CRESTOR to other people, even if they have the same medical condition you have. It may harm them.

You can ask your pharmacist or doctor for information about CRESTOR that is written for health professionals.

What are the Ingredients in CRESTOR?

Active Ingredient: rosuvastatin as rosuvastatin calcium

Inactive Ingredients: crospovidone NF, hypromellose NF, lactose monohydrate NF, magnesium stearate NF, microcrystalline cellulose NF, red ferric oxide NF, titanium dioxide USP, triacetin NF, tribasic calcium phosphate NF and yellow ferric oxide.

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Wilmington, DE 19850
For more information, go to the CRESTOR website at www.crestor.com or call 1-800-CRESTOR

This Patient Information has been approved by the U.S. Food and Drug Administration Revised 01/2023