Front

Crestat EZ®

(Rosuvastatin + Ezetimibe)
Tablet

کریسٹیٹ ایزی

COMPOSITION:
Crestat EZ 5/10 mg Tablet:
Each Bilayer film coated tablet contains:
Rosuvastatin Calcium equivalent to
Rosuvastatin ..... 5 mg.
Ezetimibe ..... 10 mg.

Product Specs.: Innovator

Crestat EZ 10/10 mg Tablet:
Each Bilayer film coated tablet contains:
Rosuvastatin Calcium equivalent to
Rosuvastatin ..... 10 mg.
Ezetimibe ..... 10 mg.

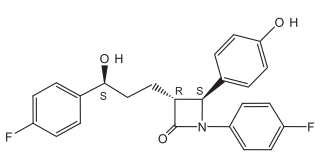
Product Specs.: Innovator

Crestat EZ 20/10 mg Tablet:
Each Bilayer film coated tablet contains:
Rosuvastatin Calcium equivalent to
Rosuvastatin ..... 20 mg.
Ezetimibe ..... 10 mg.

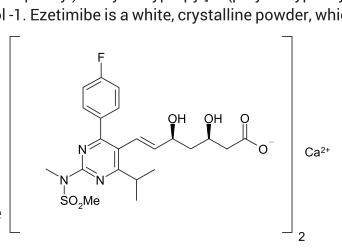
Product Specs.: Innovator

DESCRIPTION:
Each tablet of "Brand Name "contains rosuvastatin calcium and ezetimibe.
Rosuvastatin is a 3-hydroxy-3¬ methylglutaryl coenzyme A (HMG CoA)-reductase inhibitor. Ezetimibe is a dietary cholesterol absorption inhibitor. The chemical name of ezetimibe is (3R,4S)-1-(p-Fluorophenyl)-3-[(3S)-3-(p-fluorophenyl)-3¬ hydroxypropyl]-4-(p-hydroxyphenyl)-2-azetidinone. The empirical formula is $C_{24}H_{21}F_2NO_3$. Its molecular weight is 409.43 g.mol -1. Ezetimibe is a white, crystalline powder, which is insoluble in water. Its structural formula is:

Rosuvastatin



Ezetimibe



The chemical name for rosuvastatin calcium is bis[(E)-7-[4-(4-fluorophenyl)-6-isopropyl2[methyl(methyl sulfonyl)amino] pyrimidin-5-yl] (3R,5S)-3,5-dihydroxyhept-6-enoic acid] calcium salt to [S-[R*,S*-(E)]]-7-[4-(4-Fluorophenyl)-6-(1-methylethyl)-2-[methyl(methylsulfonyl)amino]-5¬ pyrimidinyl]-3,5-dihydroxy-6-heptenoic acid, calcium salt (2:1). The empirical formula for rosuvastatin calcium is $(C_{22}H_{27}FN_3O_6S)2Ca$ and the molecular weight is 1001.14 g.mol-1.

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. Its structural formula is: Rosuvastatin / Ezetimibe tablets 5 mg/10 mg, 10 mg/10 mg, and 20 mg/10 mg contain the equivalent of 5, 10, 20, and rosuvastatin (provided as rosuvastatin calcium 5.2, 10.4, 20.8, and 41.7 mg) and 10 mg ezetimibe.

CLINICAL PHARMACOLOGY:
Mechanism of Action:
Rosuvastatin: Rosuvastatin is an inhibitor of HMG CoA-reductase, the rate-limiting enzyme that converts 3-hydroxy3-methylglutaryl coenzyme A to mevalonate, a precursor of cholesterol. In in vivo and in vitro studies, rosuvastatin produces its lipid-modifying effects in two ways. First, it increases the number of hepatic LDL receptors on the cell-surface to enhance uptake and catabolism of LDL. Second, rosuvastatin inhibits hepatic synthesis of VLDL, which reduces the total number of VLDL and LDL particles.
Ezetimibe: The molecular target of ezetimibe is the sterol transporter, Niemann-Pick C1-Like 1 (NPC1L1), which is involved in the intestinal uptake of cholesterol and phytosterols. Ezetimibe localizes at the brush border of the small intestine and inhibits the absorption of cholesterol, leading to a decrease in the delivery of intestinal cholesterol to the liver. This causes a reduction of hepatic cholesterol stores and an increase in clearance of cholesterol from the blood.
Pharmacodynamics:
The maximum therapeutic response of rosuvastatin is usually achieved by 4 weeks and is maintained after that. The maximum therapeutic response of ezetimibe is generally achieved within 2 weeks and is maintained during chronic therapy.

Pharmacokinetics:
Absorption:
Rosuvastatin: In clinical pharmacology studies in man, peak plasma concentrations of rosuvastatin were reached 3 to 5 hours following oral dosing. Both Cmax and AUC increased in approximate proportion to rosuvastatin dose. The absolute bioavailability of rosuvastatin is approximately 20%. The AUC of rosuvastatin does not differ following evening or morning drug administration. Administration of rosuvastatin with food did not affect the AUC of rosuvastatin.
Ezetimibe: After oral administration, ezetimibe is absorbed and extensively conjugated to a pharmacologically active phenolic glucuronide (ezetimibe-glucuronide). After a single 10-mg dose of ezetimibe to fasted adults, mean ezetimibe peak plasma concentrations (Cmax) of 3.4 to 5.5 ng/mL were attained within 4 to 12 hours (Tmax). Ezetimibe-glucuronide mean Cmax values of 45 to 71 ng/mL were achieved between 1 and 2 hours (Tmax). There was no substantial deviation from dose proportionality between 5 and 20 mg. The absolute bioavailability of ezetimibe cannot be determined, as the compound is virtually insoluble in aqueous media suitable for injection. Concomitant food administration (high-fat or non-fat meals) had no effect on the extent of absorption of ezetimibe when administered as ezetimibe 10-mg tablets. The Cmax value of ezetimibe was increased by 38% with consumption of high-fat meals.
Distribution:
Rosuvastatin: 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.
Ezetimibe:
Ezetimibe and ezetimibe-glucuronide are highly bound (>90%) to human plasma proteins.
Elimination:
Rosuvastatin: 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. Following oral administration, rosuvastatin and its metabolites are primarily excreted in the feces (90%). The elimination half-life (t1/2) of rosuvastatin is approximately 19 hours. After an intravenous dose, approximately 28% of total body clearance was via the renal route, and 72% by the hepatic route.
Ezetimibe: Ezetimibe is primarily metabolized in the small intestine and liver via glucuronide conjugation with subsequent biliary and renal excretion. In humans, ezetimibe is rapidly metabolized to ezetimibe-glucuronide. Ezetimibe and ezetimibe- glucuronide are the major drug-derived compounds detected in plasma, constituting approximately 10 to 20% and 80 to 90% of the total drug in plasma, respectively. Both ezetimibe and ezetimibe-glucuronide are eliminated from plasma with a half-life of approximately 22 hours for both ezetimibe and ezetimibe-glucuronide. Plasma concentration-time profiles exhibit multiple peaks, suggesting enterohepatic recycling.

Specific Populations:
Geriatric Patients:
Rosuvastatin: There were no differences in plasma concentrations of rosuvastatin between the non-elderly and elderly populations (age ⩾ 65 years).
Ezetimibe: Plasma concentrations for total ezetimibe are 2-fold higher in older (⩾65 years) healthy subjects compared to younger subjects.
Gender:
Rosuvastatin: There were no differences in plasma concentrations of rosuvastatin between men and women.
Ezetimibe: In a multiple-dose study with ezetimibe given 10 mg once daily for 10 days, plasma concentrations for total ezetimibe were slightly higher (<20%) in women than in men.
Hepatic Impairment:
Rosuvastatin: In patients with chronic alcohol liver disease, plasma concentrations of rosuvastatin were modestly increased. In patients with Child-Pugh A disease, Cmax and AUC were increased by 60% and 5%, respectively, as compared with patients with normal liver function. In patients with Child-Pugh B disease, Cmax and AUC were increased 100% and 21%, respectively, compared with patients with normal liver function
Ezetimibe: After a single 10-mg dose of ezetimibe, the mean AUC for total ezetimibe was increased approximately 1.7-fold in patients with mild hepatic impairment (Child-Pugh score 5 to 6), compared to healthy subjects. The mean AUC values for total ezetimibe and ezetimibe increased approximately 3- to 4-fold and 5- to 6- fold, respectively, in patients with moderate (Child-Pugh score 7 to 9) or severe hepatic impairment (Child- Pugh score 10 to 15). In a 14-day, multiple-dose study (10 mg daily) in patients with moderate hepatic impairment, the mean AUC for total ezetimibe and ezetimibe increased approximately 4-fold on both Day 1 and Day 14 when compared to healthy subjects.
Renal Impairment:
Rosuvastatin: MMild to moderate renal impairment (CLcr ⩾30 mL/min/1.73 m2) 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 (CLcr 80 mL/min/1.73 m2). Steady-state plasma concentrations of rosuvastatin in patients on chronic hemodialysis were approximately 50% greater compared with healthy volunteer subjects with normal renal function.
Ezetimibe: After a single 10-mg dose of ezetimibe in patients with severe renal disease (n=8; mean CLcr⩽ 30 mL/min/1.73 m2), the mean AUC values for total ezetimibe, ezetimibe-glucuronide, and ezetimibe were increased approximately 1.5-fold, compared to healthy subjects (n=9).

DRUG INTERACTIONS:
No clinically significant pharmacokinetic interaction was seen when ezetimibe was co-administered with rosuvastatin. Cytochrome P450 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).
Ezetimibe is neither an inhibitor nor an inducer of these cytochrome P450 isozymes.

INDICATIONS AND USAGE:
- ***Indicated in adults:***
- As an adjunct to diet in patients with primary non-familial hyperlipidemia to reduce low-density lipoprotein cholesterol (LDL-C).
- Alone or as an adjunct to other LDL-C-lowering therapies in patients with homozygous familial hypercholesterolemia (HoFH) to reduce LDL-C.

DOSAGE AND ADMINISTRATION:
Recommended Dosage and Administration Information:
- Swallow tablets whole at any time of day, with or without food. Do not crush, dissolve, or chew tablets.
- The dosage range is 5 mg/10 m g to 20 mg/10 mg once daily.
- The recommended dose depends on a patient's indication for usage, LDL-C, and individual risk for cardiovascular events.
- The starting dosage for patients switching from co-administration of a statin and ezetimibe is based on an equivalent dose of rosuvastatin and 10 mg of ezetimibe.
- Assess LDL-C when clinically appropriate, as early as 2 weeks after initiating and adjust the dosage if necessary.

Recommended Dosage in Asian Patients: Initiate at 5 mg/10 mg daily due to increased rosuvastatin plasma concentrations. Consider the risk/benefit when treating Asian patients not adequately controlled at doses up to 20 mg/10 mg once daily
Recommended Dosage in Patients with Renal Impairment: In patients with severe renal impairment (CLcr less than 30 mL/min/1.73 m2) not on hemodialysis, the recommended starting dosage is 5 mg/10 mg once daily and should not exceed 10 mg/10 mg once daily There are no dosage adjustment recommendations for patients with mild and moderate renal impairment.

DOSAGE AND ADMINISTRATION MODIFICATIONS DUE TO DRUG INTERACTIONS:
In patients taking a bile acid sequestrant, administer at least 2 hours before or 4 hours after the bile acid sequestrant
- When taking with an aluminum and magnesium hydroxide combination antacid, administer at least 2 hours before the antacid
- Concomitant use with the following drugs requires dosage modifications
- Darolutamide: Do not exceed 5 mg/10 mg once daily.
- Regorafenib: Do not exceed 10 mg/10 mg once daily.
- Antivirals :Concomitant use of sofosbuvir/velpatasvir/voxilaprevir and ledipasvir/sofosbuvir is not recommended. In patients taking simeprevir, dasabuvir/ombitasvir/paritaprevir/ritonavir, elbasvir/grazoprevir, sofosbuvir/velpatasvir, glecaprevir/pibrentasvir, atazanavir/ritonavir, and lopinavir/ritonavir initiate at 5 mg/10 mg once daily. Do not exceed 10 mg/10 mg once daily. No dose adjustment is needed for concomitant use with fosamprenavir/ritonavir or tipranavir/ritonavir

CONTRAINDICATIONS:
Contraindicated in patients with:
- Acute liver failure or decompensated cirrhosis.
- Hypersensitivity to rosuvastatin, ezetimibe, or any excipients. Hypersensitivity reactions including anaphylaxis, angioedema, and erythema multiforme have been reported.

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WARNINGS AND PRECAUTIONS:

Myopathy and Rhabdomyolysis: May cause myopathy (muscle pain, tenderness, or weakness with creatine kinase [CK] above ten times the upper limit of normal) and rhabdomyolysis. Acute kidney injury secondary to myoglobinuria and rare fatalities have occurred as a result of rhabdomyolysis with statins, including rosuvastatin.

Risk Factors for Myopathy: Risk factors for myopathy include age 65 years or greater, uncontrolled hypothyroidism, renal impairment, concomitant use with certain other drugs including other lipid-lowering therapies, and higher; Asian patients may be at higher risk for myopathy. The myopathy risk is greater in patients taking 20 mg/10 mg daily compared with lower dosages.

Steps to Prevent or Reduce the Risk of Myopathy and Rhabdomyolysis: The concomitant use with cyclosporine or gemfibrozil is not recommended. Dosage modifications are recommended for patients taking certain antiviral medications, Darolutamide, and Niacin, fibrates, and colchicine may also increase the risk of myopathy and rhabdomyolysis. Discontinue if markedly elevated CK levels occur or myopathy is diagnosed or suspected. Muscle symptoms and CK increases may resolve if discontinued. Temporarily discontinue in patients experiencing an acute or serious condition at high risk of developing renal failure secondary to rhabdomyolysis, e.g., sepsis; shock; severe hypovolemia; major surgery; trauma; severe metabolic, endocrine, or electrolyte disorders; or uncontrolled epilepsy. Inform patients of the risk of myopathy and rhabdomyolysis when starting or increasing the dosage. Instruct patients to promptly report any unexplained muscle pain, tenderness or weakness, particularly if accompanied by malaise or fever.

Immune-Mediated Necrotizing Myopathy: There have been rare reports of immune-mediated necrotizing myopathy (IMNM), an autoimmune myopathy, associated with statin use. IMNM is characterized by: proximal muscle weakness and elevated serum creatine kinase, which persist despite discontinuation of statin treatment; positive anti-HMG CoA reductase antibody; muscle biopsy showing necrotizing myopathy; and improvement with immunosuppressive agents. Additional neuromuscular and serologic testing may be necessary. Treatment with immunosuppressive agents may be required. Consider risk of IMNM carefully prior to initiation of a different statin. If therapy is initiated with a different statin, monitor for signs and symptoms of IMNM.

Hepatic Dysfunction: Increases in serum transaminases have occurred with rosuvastatin. In most cases, the elevations 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. Marked persistent increases of hepatic transaminases also occur with rosuvastatin. There have been rare post marketing reports of fatal and non-fatal hepatic failure in patients taking statins, including rosuvastatin. Patients who consume substantial quantities of alcohol and/or have a history of liver disease may be at increased risk for hepatic injury. Consider liver enzyme testing before initiation and thereafter, when clinically indicated. Contraindicated in patients with acute liver failure or decompensated cirrhosis. If serious hepatic injury with clinical symptoms and/or hyperbilirubinemia or jaundice occurs, promptly discontinue.

Proteinuria and Hematuria: Consider a dose reduction for patients on therapy with unexplained persistent proteinuria and/or hematuria during routine urinalysis testing.

Increases in HbA1c and Fasting Serum Glucose Levels: Increases in HbA1c and fasting serum glucose levels have been reported with statins, including rosuvastatin, in some instances these increases may exceed the threshold for the diagnosis of diabetes mellitus. Optimize lifestyle measures, including regular exercise, maintaining a healthy body weight, and making healthy food choices.

ADVERSE REACTIONS:

Most common adverse reactions for:

- Rosuvastatin (incidence >2% and greater than placebo) are headache, nausea, myalgia, arthralgia, dizziness, asthenia, constipation, and abdominal pain.
- Ezetimibe (incidence >2% and greater than placebo) are upper respiratory tract infection, diarrhea, arthralgia, sinusitis, pain in extremity, fatigue, and influenza.
- Ezetimibe co-administered with a statin (incidence >2% and greater than statin alone) are nasopharyngitis, myalgia, upper respiratory tract infection, arthralgia, diarrhea, back pain, influenza, pain in extremity, and fatigue.

Post-marketing Experience: The following adverse reactions have been identified during post-approval use of rosuvastatin and ezetimibe. Because these reactions are reported voluntarily from a population of uncertain size, it is generally not possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Rosuvastatin: Arthralgia, fatal and non-fatal hepatic failure, hepatitis, jaundice, thrombocytopenia, depression, sleep disorders (including insomnia and nightmares), peripheral neuropathy, interstitial lung disease and gynecomastia. There have been rare reports of immune-mediated necrotizing myopathy associated with statin use. There have been rare post marketing reports of cognitive impairment (e.g., memory loss, forgetfulness, amnesia, memory impairment, confusion) associated with statin use. These cognitive issues have been reported for all statins. The reports are generally nonserious, and reversible upon statin discontinuation, with variable times to symptom onset (1 day to years) and symptom resolution (median of 3 weeks).

Ezetimibe: Hypersensitivity reactions, including anaphylaxis, angioedema, rash, and urticaria; erythema multiforme; arthralgia; myalgia; elevated creatine phosphokinase; myopathy/rhabdomyolysis; elevations in liver transaminases; hepatitis; abdominal pain; thrombocytopenia; pancreatitis; nausea; dizziness; paresthesia; depression; headache; cholelithiasis; cholecystitis.

DRUG INTERACTIONS:

Drug Interactions that Increase the Risk of Myopathy and Rhabdomyolysis: 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 and instructions for preventing or managing them.

Table 5: Drug Interactions that Increase the Risk of Myopathy and Rhabdomyolysis with Rosuvastatin / Ezetimibe

Cyclosporine or Gemfibrozil	
Clinical Impact:	Cyclosporine increased rosuvastatin exposure 7-fold. In addition, ezetimibe and cyclosporine used concomitantly can increase exposure to both ezetimibe and cyclosporine. 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 cyclosporine or gemfibrozil with Rosuvastatin / Ezetimibe
Intervention:	Avoid concomitant use of cyclosporine or gemfibrozil with Rosuvastatin / Ezetimibe.
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:	Avoid concomitant use of sofosbuvir/velpatasvir/voxilaprevir and ledipasvir/sofosbuvir with Rosuvastatin / Ezetimibe. In patients taking simeprevir, dasabuvir/ombitasvir/paritaprevir/ritonavir, elbasvir/grazoprevir, sofosbuvir/velpatasvir, glecaprevir/pibrentasvir, atazanavir/ritonavir, and lopinavir/ritonavir initiate with a dose of Rosuvastatin / Ezetimibe 5 mg/10mg once daily, and do not exceed a dose of Rosuvastatin / Ezetimibe 10 mg/10 mg once daily. No dose adjustment is needed for concomitant use with fosamprenavir/ritonavir or tipranavir/ritonavir. Monitor all patients for signs and symptoms of myopathy, particularly during initiation of therapy and during upward titration of either drug.
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 Rosuvastatin / Ezetimibe 5 mg/10 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 Rosuvastatin / Ezetimibe 10 mg/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 Rosuvastatin / Ezetimibe.
Intervention:	Consider if the benefit of using fibrates concomitantly with Rosuvastatin / Ezetimibe 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 niacin with rosuvastatin.
Intervention:	Consider if the benefit of using niacin concomitantly with Rosuvastatin / Ezetimibe 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 Rosuvastatin / Ezetimibe
Intervention:	Consider if the benefit of using colchicine concomitantly with Rosuvastatin / Ezetimibe 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.

Intervention:	In patients taking antacid, administer Rosuvastatin / Ezetimibe 2 hours after the antacid

Table 7: Rosuvastatin / Ezetimibe Effects on Other Drugs

Warfarin	
Clinical Impact:	Rosuvastatin significantly increased the INR in patients receiving coumarin anticoagulants
Intervention:	In patients taking warfarin, obtain an INR before starting Rosuvastatin / Ezetimibe 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.

Pregnancy:

Risk Summary: Discontinue when pregnancy is recognized. Alternatively, consider the ongoing therapeutic needs of the individual patient. Decrease synthesis of cholesterol and possibly other biologically active substances derived from cholesterol; therefore, may cause fetal harm when administered to pregnant patients based on the mechanism of action. 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.

Lactation:

Risk Summary: There is no available information on the effects of the drug on the breastfed infant or the effects of the drug on milk production. There is no information about the presence of ezetimibe in human milk. There is no information about the effects of ezetimibe on the breastfed infant or the effects of ezetimibe on milk production. 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.

Pediatric Use: The safety and effectiveness have not been established in pediatric patients.

Geriatric Use: Advanced age (⩾65 years) is a risk factor for myopathy and rhabdomyolysis. Dose selection for an elderly patient should be cautious, recognizing the greater frequency of decreased hepatic, renal, or cardiac function; of concomitant disease or other drug therapy; and the higher risk of myopathy. Monitor geriatric patients for the increased risk of myopathy

Renal Impairment: Renal impairment is a risk factor for myopathy and rhabdomyolysis. Monitor patients with renal impairment for development of myopathy. In patients with severe renal impairment not on hemodialysis, the recommended starting dosage is 5 mg/10 mg daily and should not exceed 10 mg/10 mg daily.

Rosuvastatin: Rosuvastatin exposure is not influenced by mild to moderate renal impairment (CLcr⩾ 30 mL/min/1.73 m²). Exposure to rosuvastatin is increased to a clinically significant extent in patients with severe renal impairment.

Hepatic Impairment: Contraindicated in patients with acute liver failure or decompensated cirrhosis.

Asian Population: Pharmacokinetic studies have demonstrated an approximate 2-fold increase in median exposure to rosuvastatin in Asian subjects when compared with Caucasian controls. Adjust the dosage in Asian patients

OVERDOSAGE:

No specific treatments of over dosage are known. Hemodialysis does not significantly enhance clearance of rosuvastatin.

INSTRUCTIONS:

- Store below 30ºC.
- Protect from heat, sunlight and moisture.
- Keep out of the reach of children.
- To be sold on the prescription of a registered medical practitioner only.

PRESENTATION:

Crestat EZ 5/10 mg Tablet	:	Pack of 1 x 10 tablets.
Crestat EZ 10/10 mg Tablet	:	Pack of 1 x 10 tablets.
Crestat EZ 20/10 mg Tablet	:	Pack of 1 x 10 tablets.

ہدایات:

۳۰ درجہ سینٹی گریڈ سے کم درجہ حرارت پر رکھیں۔

گرمی، دھوپ اور نمی سے بچائیں۔

بچوں کی پہنچ سے دور رکھیں۔

صرف مستند ڈاکٹر کے نسخہ پر فروخت کریں۔

FOR FURTHER INFORMATIONS PLEASE CONTACT:

CCL

Manufactured by:
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