NoChol

(ROSUVASTATIN)

5mg, 10mg & 20mg Tablets

نوکول

۵ ملی گرام، ۱۰ ملی گرام اور ۲۰ ملی گرام گولیاں

DESCRIPTION:
NOCHOL (Rosuvastatin), a synthetic lipid-lowering agent for oral administration. Rosuvastatin calcium is bis[(E)-7-[4-(4-fluorophenyl)-6-isopropyl-2-[methyl(methylsulfonyl)amino] pyridimin-5-yl](3R,5S)-3,5-dihydroxyhept-6-enoic acid] calcium salt. The molecular formula for rosuvastatin calcium is $(C_{22}H_{27}FN_3O_6S)_2Ca$. evidence of active inflammation and fibrosis.

QUANTITATIVE & QUALITATIVE COMPOSITION:
NOCHOL (Rosuvastatin) is available for oral administration as:

1- NOCHOL Tablets 5mg
Each film coated tablet contains:
Rosuvastatin Calcium USP equivalent to Rosuvastatin.....5mg
(Product Specs.: USP)

2- NOCHOL Tablets 10mg
Each film coated tablet contains:
Rosuvastatin Calcium USP equivalent to Rosuvastatin.....10mg
(Product Specs.: USP)

3- NOCHOL Tablets 20mg
Each film coated tablet contains:
Rosuvastatin Calcium USP equivalent to Rosuvastatin.....20mg
(Product Specs.: USP)

CLINICAL PHARMACOLOGY:
MECHANISM OF ACTION:
Rosuvastatin is a selective and competitive inhibitor of HMG-CoA reductase, the rate-limiting enzyme that converts 3-hydroxy-3-methylglutaryl coenzyme A to mevalonate, a precursor for cholesterol. The primary site of action of rosuvastatin is the liver, the target organ for cholesterol lowering.
Rosuvastatin produces its lipid-modifying effects in two ways;
1.It increases the number of hepatic LDL receptors on the cell-surface, enhancing uptake and catabolism of LDL.
2.It inhibits the hepatic synthesis of VLDL, thereby reducing the total number of VLDL and LDL particles.

PHARMACOKINETICS:
Absorption:
Maximum plasma concentration is achieved approximately in 5 hours after oral administration. The absolute bioavailability is approximately 20%. Food did not affect the AUC of rosuvastatin.
Distribution:
The volume of distribution of rosuvastatin is approximately 134 L. Approximately 90% of rosuvastatin is bound to plasma proteins, mainly to albumin. This binding is reversible and independent of plasma concentrations.
Metabolism:
Rosuvastatin undergoes limited metabolism (approximately 10%) by CYP2C9. The main metabolites are N-desmethyl metabolite (50% less active than rosuvastatin) and lactone (clinically inactive). Rosuvastatin accounts for greater than 90% of the circulating HMG-CoA reductase inhibitor activity.
Excretion:
About 90% of an oral dose is excreted in the faeces and the remainder is excreted in the urine. The elimination half-life is approximately 19 hours.
Special Populations:
Renal Insufficiency:
Plasma concentrations of rosuvastatin increased (about 3-fold) in patients with severe renal impairment. There is 50% increase in steady-state plasma concentrations of rosuvastatin in patients undergoing haemodialysis.
Hepatic Insufficiency:
In patients with chronic alcohol liver disease, plasma concentrations of rosuvastatin were modestly increased.

THERAPEUTIC INDICATIONS:
NOCHOL is indicated for the treatment of:
1. Hyperlipidemia and Mixed Dyslipidemia:
As adjunctive therapy to diet to reduce elevated Total-C, LDL-C, ApoB, nonHDL-C, and triglycerides and to increase HDL-C in adult patients with primary hyperlipidemia or mixed dyslipidemia. Lipid altering agents should be used in addition to a diet restricted in saturated fat and cholesterol when response to diet and nonpharmacological interventions alone has been inadequate.
2. Pediatric Patients 10 to 17 years of age with Heterozygous Familial Hypercholesterolemia (HeFH):
Adjunct to diet to reduce Total-C, LDL-C and ApoB levels in adolescent boys and girls, who are at least one year postmenarche, 10-17 years of age with heterozygous familial hypercholesterolemia if after an adequate trial of diet therapy the following findings are present: LDL-C >190 mg/dl or >160 mg/dl and there is a positive family history of premature cardiovascular disease (CVD) or two or more other CVD risk factors.
3. Hypertriglyceridemia:
Adjunct to diet for the treatment of adult patients with hypertriglyceridemia.
4. Primary Dysbetalipoproteinemia:
Adjunct to diet for the treatment of patients with primary dysbetalipoproteinemia (Type III Hypertriglyceridemia).
5. Homozygous Familial Hypertriglyceridemia
Adjunctive therapy to other lipid lowering treatments (e.g., LDL apheresis) or alone if such treatments are unavailable to reduce LDL-C Total-C, and ApoB in adult patients with homozygous familial hypertriglyceridemia
6. Slowing of the Progression of Atherosclerosis
Adjunct 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.
7. Prevention of Cardiovascular Events
Prevention of major cardiovascular events in patients who are estimated to have a high risk for a first cardiovascular event, as an adjunct correction of other risk factors.

DOSAGE AND ADMINISTRATION:
The dose range for **NOCHOL** is 5mg to 40mg orally once daily. The usual starting dose is 10-20mg.
NOCHOL can be administered as a single dose at any time of day, with or without food.
When initialing **NOCHOL** therapy or switching from another HMG-CoA reductase inhibitor therapy, the appropriate **NOCHOL** starting dose should first be utilized, and only then titrated according to the patient's response and individualized goal of therapy. After initiation or upon titration of **NOCHOL**, lipid levels should be analyzed within 2 to 4 weeks and the dosage adjusted accordingly.
The 40mg dose of **NOCHOL** should be used only for those patients who have not achieved their LDL-C goal utilizing the 20mg.
Heterozygous Familial Hypercholesterolemia in Pediatric Patients (10 to 17 years):
The usual dose range of **NOCHOL** is 5mg/day to 20mg/day; the maximum recommended dose is 20mg /day. Doses should be individualized according to the recommended goal of therapy. Adjustments should be made at intervals of 4 weeks or more.
Homozygous Familial Hypercholesterolemia:
The recommended starting dose of **NOCHOL** is 20mg/day. Response to therapy should be estimated from pre-apheresis LDL-C levels.

Special Population:
Elderly:
Starting dose of 5 mg is recommended in patients >70 years.
Renal Insufficiency:
The recommended start dose is 5mg in patients with moderate renal insufficiency (creatinine clearance <60mL/min).
Patients with pre-disposing factors to myopathy:
The recommended start dose is 5mg. The dose may be increased at intervals of 4 weeks, if necessary, to a usual maximum of 20mg/day.

CONTRAINDICATIONS:
Rosuvastatin is contraindicated:
- In patients with hypersensitivity to rosuvastatin or to any of the excipients.
- In patients with active liver disease including unexplained, persistent elevation of serum transaminases.
- In patients with severe renal insufficiency (Creatinine clearance <30mL/min.)
- In patients with myopathy.
- In patients receiving concomitant cyclosporine.
- In children younger than 10 years.
- Concomitant use of protease inhibitors in HIV patients.

The 40mg dose is contraindicated in patients with pre-disposing factors for myopathy/rhabdomyolysis .
Such factors include:
- Creatinine clearance <60mL/min.
- Hypothyroidism.
- History of hereditary muscular disorders.
- History of muscular toxicity with another HMG-CoA reductase inhibitor or fibrate.
- Alcohol abuse.
- Situations where an increase in plasma levels may occur.
- Concomitant use of fibrates.
- Asian patients.

PRECAUTIONS:
- Monitoring of serum transaminase levels taken into account and if persistently increase in serum transaminase levels is observed, discontinued **NOCHOL.**
- A dose reduction should be considered if unexplained persistent proteinuria and/or hematuria is suspected.

Use NOCHOL with caution;
- In patients with pre-disposing factor for myopathy/rhabdomyolysis, In patients who consume substantial quantities of alcohol and/or have a history of chronic liver disease, With drugs that may decrease the levels of endogenous steroid hormones such as ketoconazole, spironolactone, and cimetidine to avoid increase in HbA1c and fasting serum glucose levels.

Pregnancy & Lactation:
Contraindicated in pregnancy and during lactation.

DRUG INTERACTIONS:
Coumarin
In patients taking coumarin anticoagulants and rosuvastatin concomitantly, INR should be determined before starting rosuvastatin and frequently enough during early therapy to ensure that no significant alteration of INR occurs.
Gemfibrozil:
Gimfibrozil significantly increased rosuvastatin exposure. Therefore combination therapy should be avoided. If used, do not exceed rosuvastatin 10mg once daily.
Antacid:
The simultaneous dosing of rosuvastatin with an antacid suspension decreases 50% rosuvastatin plasma concentration. The antacid should be taken atleast 2 hours after rosuvastatin administration.
Niacin:
Reduction in rosuvastatin dosage should be considered when used with niacin to avoid risk of skeletal muscle effects.

ADVERSE REACTIONS:
- Rhabdomyolosis with myoglobinuria and acute renal failure and myopathy (including myositis)
- Liver enzymes abnormalities.

Adverse reactions that led to treatment discontinuation were myalgia, abdominal, pain and nausea.
Common:
Headache, constipation, nausea, abdominal pain, myalgia, asthenia, diabetic mellitus.

OVERDOSAGE:
In the event of overdose, the patient should be treated symptomatically and supportive measures instituted as required. Liver function and creatinine kinase levels should be monitored.

INSTRUCTIONS:
- Store below 30˚C.
- Protect from light & moisture.
- Keep out of reach of children.

To be sold on prescription of a registered medical practitioner.

HOW SUPPLIED:
NOCHOL (Rosuvastatin) Tablets 5mg are available in pack of 10's.
NOCHOL (Rosuvastatin) Tablets 10mg are available in pack of 10's.
NOCHOL (Rosuvastatin) Tablets 20mg are available in pack of 10's.

خوراک: ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔
ہدایت: دوا کو کم ڈگری سینٹی گریڈ سے کم درجہ حرارت پر رکھیں۔
دوا کو بچوں سے بچا کر رکھیں۔ بچوں کی پہنچ سے دور رکھیں۔
صرف رجسٹرڈ ڈاکٹر کے نسخے کے مطابق فروخت کریں۔

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