SUMMARY OF PRODUCT CHARACTERISTICS

1. Name of the medicinal product

Rostat EZ 20mg Tablets

2. Qualitative and quantitative composition

Each film coated tablet contains:

Rosuvastatin Calcium USP Equivalent to Rosuvastatin 20mg

Ezetimibe USP 10mg

For the full list of excipients, see section 6.1

3. Pharmaceutical form

A pink colour circular shape biconvexed film coated tablet, scored in the middle on one side and plain on other side.

4. Clinical particulars

4.1 Therapeutic indications

Rosuvastatin+Ezetimibe is used in the treatment of high cholesterol. Rosuvastatin is a lipid-lowering medicine which prevents your body from making "bad" cholesterol (LDL) while raising "good" cholesterol (HDL) levels. Ezetimibe is a cholesterol absorption inhibitor which prevents absorption of cholesterol from the intestines.

4.2 Posology and method of administration

Posology

The recommended dose of Rostat EZ depends on a patients indication for usage, LDLC, and individual risk for cardiovascular events.Initiate Rostat EZ 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 m^2) not on hemodialysis, the recommended starting dosage is 5 mg/10 mg once daily and should not exceed 10 mg/10 mg once daily

Method of administration

Rostat EZ is for oral administration. Rostat EZ can be administered as a single dose at any time of the day, with or without food.

Pediatric Use

The safety and effectiveness of Rostat EZ have not been established in pediatric patients.

4.3 Contraindications

Hypersensitivity to rosuvastatin, ezetimibe, or any excipients in Rostat EZ. Hypersensitivity reactions including anaphylaxis, angioedema, and erythema multiforme have been reported

4.4 Special warnings and precautions for use

Myopathy/Rhabdomyolosis

In post-marketing experience with ezetimibe, cases of myopathy and rhabdomyolysis have been reported. Most patients who developed rhabdomyolysis were taking a statin concomitantly with ezetimibe.
However, rhabdomyolysis has been reported very rarely with ezetimibe monotherapy and very rarely with the addition of ezetimibe to other agents known to be associated with increased risk of rhabdomyolysis.

The concomitant use of Rostat EZ with cyclosporine or gemfibrozil is not recommended. Rostat EZ dosage modifications are recommended for patients taking certain antiviral medications, darolutamide, and regorafenib. Niacin, fibrates, and colchicine may also increase the risk of myopathy and rhabdomyolysisRostat EZ should be prescribed with caution in patients with pre-disposing factors for rhabdomyolysis. A CPK level should be measured before starting treatment in the following situations:

Increases in HbA1c and fasting serum glucose levels have been reported with statins, including rosuvastatin. Based on clinical trial data with rosuvastatin, in some instances these increases may exceed the threshold for the diagnosis of diabetes mellitus.

4.5 Interaction with other medicinal products and other forms of interaction

In patients taking a bile acid sequestrant, administer Rostat EZ at least 2 hours before or 4 hours after the bile acid sequestrant.
When taking Rostat EZ with an aluminum and magnesium hydroxide combination antacid, administer Rostat EZ at least 2 hours before the antacid. Concomitant use of sofosbuvir/velpatasvir/voxilaprevir and ledipasvir/sofosbuvir with Rostat EZ is not recommended. In patients taking simeprevir, dasabuvir/ombitasvir/paritaprevir/ritonavir, elbasvir/grazoprevir, sofosbuvir/velpatasvir, glecaprevir/pibrentasvir, atazanavir/ritonavir, and lopinavir/ritonavir initiate Rostat EZ at 5 mg/10 mg once daily. Do not exceed Rostat EZ 10 mg/10 mg once daily.

No dose adjustment is needed for concomitant use with fosamprenavir/ritonavir or tipranavir/ritonavir.

4.6 Fertility, Pregnancy and lactation

Pregnancy

Discontinue Rostat EZ when pregnancy is recognized. Alternatively, consider the ongoing therapeutic needs of the individual patient. Rostat EZ decreases synthesis of cholesterol and possibly other biologically active substances derived from cholesterol; therefore, Rostat EZ may cause fetal harm when administered to pregnant patients
Breast-feeding

Rostat EZ, decrease cholesterol synthesis and possibly the synthesis of other biologically active substances derived from cholesterol and may cause harm to the breastfed infant.

4.7 Effects on ability to drive and use machines

Rostat EZ has negligible influence on the ability to drive and use machines. However, when driving vehicles or operating machines, it should be taken into account that dizziness has been reported.

4.8 Undesirable effects

Reporting of suspected adverse reactions

Reporting of suspected adverse reactions: Healthcare professionals are asked to report any suspected adverse reactions via pharmacy and poisons board, Pharmacovigilance Electronic Reporting System (PvERS) https://pv.pharmacyboardkenya.org

Nausea, Weakness, Muscle pain, Headache, Joint pain, Diarrhea, Abdominal pain, Common cold, Upper respiratory tract infection.

4.9 Overdose

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

5. Pharmacological properties

5.1 Pharmacodynamic properties

Rosuvastatin is an inhibitor of HMG CoA-reductase, the rate-limiting enzyme that converts 3-hydroxy3methylglutaryl coenzyme A to mevalonate, a precursor of cholesterol. 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. 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.

5.2 Pharmacokinetic properties

Absorption

In clinical pharmacology studies in man, peak plasma concentrations of rosuvastatin were reached 3 to 5 hours following oral dosing. The absolute bioavailability of rosuvastatin is approximately 20%. 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).

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. Ezetimibe and ezetimibe-glucuronide are highly bound (>90%) to human plasma proteins.

Elimination

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 onehalf 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. 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.

5.3 Preclinical safety data

There are no pre-clinical data of relevance to the prescriber.

6. Pharmaceutical particulars

6.1 List of excipients

Microcrystalline Cellulose

Maize Starch

Lactose

Povidone K30

Purified Talc

Croscarmellose Sodium

Colloidal Anhydrous Silica

Magnesium Stearate

Hypromellose E15

Titanium Dioxide

Ponceau 4R Lake

Isopropyl Alcohol

Dichloromethane

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

24 Months

6.4 Special precautions for storage

Store below 30°C. Protect from light & moisture.

6.5 Nature and contents of container

Commercial Presentation: 4's, 10's, 20's, 30's & 100's

3 x 10's (10 tablets are packed in one Alu-Alu blister and 3 such Alu-Alu blisters are kept in one carton along with package insert).

6.6. Special Precautions for disposal and other handling

Not applicable.

7. Marketing authorization holder and Manufacturing Site Addresses

Marketing authorization holder:

INNOCIA LIFESCIENCES PVT. LTD.,

Block A, No.12, Balaji Nagar, Ambattur, Chennai-600 053 Country: INDIA.

Manufacturing Site:

ATOZ Pharmaceutials Pvt.Ltd.,

No.12, Balaji Nagar, Ambattur, Chennai-600053,

India.

8. Marketing authorisation number(s)

CTD9696

9. Date of first registration

3/03/2023

10. Date of revision of the text:

18/09/2023

11. Dosimetry (If Applicable):

Not Applicable

12. Instructions for preparation of radiopharmaceuticals (If Applicable): Not Applicable