Summary of Product Characteristics for Pharmaceutical Products

1.Name of the medicinal product

ROSTAT-40 (Rosuvastatin 40mg) film coated tablets.

2.Qualitative and quantitative composition

Each film coated tablet contains

Rosuvastatin Calcium USP Equivalent to Rosuvastatin 40mg

For the full list of excipients, see section 6.1.

3.Pharmaceutical form

Tablet:

An orange color circular shape biconvexed film coated tablet, scored in the middle on one side and plain on other side of the tablet.

4. Clinical particulars

4.1 Therapeutic indications

Treatment of hypercholesterolaemia:

Adults, adolescents and children aged 6 years or older with primary hypercholesterolaemia (type IIa including heterozygous familial hypercholesterolaemia) or mixed dyslipidaemia (type IIb) as an adjunct to diet when response to diet and other non-pharmacological treatments (e.g. exercise, weight reduction) is inadequate.
Adults, adolescents and children aged 6 years or older with homozygous familial hypercholesterolaemia as an adjunct to diet and other lipid lowering treatments (e.g. LDL apheresis) or if such treatments are not appropriate.
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 to correction of other risk factors.

4.2 Posology and method of administration

Treatment of hypercholesterolaemia

The recommended start dose is 5mg or 10 mg orally once daily in both statin or patients switched from another HMG CoA reductase inhibitor. The choice of start dose should take into account the individual patient's cholesterol level and future cardiovascular risk as well as the potential risk for adverse reactions). A dose adjustment to the next dose level can be made after 4 weeks, if necessary. In light of the increased reporting rate of adverse reactions with the 40 mg dose compared to lower doses, a final titration to the maximum dose of 40 mg should only be considered in patients with severe hypercholesterolaemia at high cardiovascular risk (in particular those with familial hypercholesterolaemia), who do not achieve their treatment goal on 20 mg, and in whom routine follow-up will be performed. Specialist supervision is recommended when the 40 mg dose is initiated.
Prevention of cardiovascular events:

In the cardiovascular events risk reduction study, the dose used was 20 mg daily

Mode of Administration:
Oral.

4.3 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 elevations of serum transaminases and any serum transaminase elevation exceeding 3 times the upper limit of normal (ULN).
- in patients with severe renal impairment (creatinine clearance <30 ml/min).
- in patients with myopathy.
- in patients receiving concomitant combination of sofosbuvir/velpatasvir/voxilaprevir.
- in patients receiving concomitant ciclosporin.
- during pregnancy and lactation and in women of childbearing potential not using appropriate contraceptive measures.
- The 40 mg dose is contraindicated in patients with pre-disposing factors for myopathy/rhabdomyolysis.
- Such factors include:
- moderate renal impairment (creatinine clearance < 60 ml/min)
- hypothyroidism
- personal or family history of hereditary muscular disorders
- previous history of muscular toxicity with another HMG-CoA reductase inhibitor or fibrate - alcohol abuse
- situations where an increase in plasma levels may occur
- Asian patients
- concomitant use of fibrates

4.4 Special warnings and precautions for use

Renal Effects

Proteinuria, detected by dipstick testing and mostly tubular in origin, has been observed in patients treated with higher doses of Rosuvastatin, in particular 40 mg, where it was transient or intermittent in most cases. Proteinuria has not been shown to be predictive of acute or progressive renal disease. The reporting rate for serious renal events in post-marketing use is higher at the 40 mg dose. An assessment of renal function should be considered during routine follow-up of patients treated with a dose of 40 mg.

Skeletal Muscle Effects

Effects on skeletal muscle e.g. myalgia, myopathy and, rarely, rhabdomyolysis have been reported in Rosuvastatin-treated patients with all doses and in particular with doses > 20 mg. Very rare cases of rhabdomyolysis have been reported with the use of ezetimibe in combination with HMG-CoA reductase inhibitors. A pharmacodynamic interaction cannot be excluded and caution should be exercised with their combined use. As with other HMG-CoA reductase inhibitors, the reporting rate for rhabdomyolysis associated with Rosuvastatin in post-marketing use is higher at the 40 mg dose.

4.5 Interaction with other medicinal products and other forms of interaction

Transporter protein inhibitors: Rosuvastatin is a substrate for certain transporter proteins including the hepatic uptake transporter OATP1B1 and efflux transporter BCRP. Concomitant administration of Rosuvastatin with medicinal products that are inhibitors of these transporter proteins may result in increased rosuvastatin plasma concentrations and an increased risk of myopathy.

4.6 Fertility, Pregnancy and lactation

Rosuvastatin is contraindicated in pregnancy and lactation. Women of child bearing potential should use appropriate contraceptive measures. Since cholesterol and other products of cholesterol biosynthesis are essential for the development of the foetus, the potential risk from inhibition of HMG-CoA reductase outweighs the advantage of treatment during pregnancy. If a patient becomes pregnant during use of this product, treatment should be discontinued immediately.

4.7 Effects on ability to drive and use machines

Based on its pharmacodynamic properties, rosuvastatin is unlikely to affect this ability. When driving vehicles or operating machines, it should be taken into account that dizziness may occur during treatment.

4.8 Undesirable effects

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

Diabetes mellitus, Headache, Dizziness, Constipation, Nausea, Abdominal pain, Myalgia and Asthenia.

4.9 Overdose

There is no specific treatment in the event of overdose. In the event of overdose, the patient should be treated symptomatically and supportive measures instituted as required. Liver function and CK levels should be monitored. Haemodialysis is unlikely to be of benefit.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: HMG-CoA reductase inhibitors

ATC code: C10A A07
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 increases the number of hepatic LDL receptors on the cell-surface, enhancing uptake and catabolism of LDL and it inhibits the hepatic synthesis of VLDL, thereby reducing the total number of VLDL and LDL particles.

5.2 Pharmacokinetic properties

Absorption: Maximum rosuvastatin plasma concentrations are achieved approximately 5 hours after oral administration. The absolute bioavailability is approximately 20%.
Distribution: Rosuvastatin is taken up extensively by the liver which is the primary site of cholesterol synthesis and LDL-C clearance. The volume of distribution of rosuvastatin is approximately 134 L. Approximately 90% of rosuvastatin is bound to plasma proteins, mainly to albumin.
Metabolism: Rosuvastatin undergoes limited metabolism (approximately 10%). In vitro metabolism studies using human hepatocytes indicate that rosuvastatin is a poor substrate for cytochrome P450-based metabolism. CYP2C9 was the principal isoenzyme involved, with 2C19, 3A4 and 2D6 involved to a lesser extent. The main metabolites identified are the N-desmethyl and lactone metabolites. The Ndesmethyl metabolite is approximately 50% less active than rosuvastatin whereas the lactone form is considered clinically inactive. Rosuvastatin accounts for greater than 90% of the circulating HMG-CoA reductase inhibitor activity.
Excretion: Approximately 90% of the rosuvastatin dose is excreted unchanged in the faeces (consisting of absorbed and non-absorbed active substance) and the remaining part is excreted in urine. Approximately 5% is excreted unchanged in urine. The plasma elimination half-life is approximately 19 hours. The elimination half-life does not increase at higher doses. The geometric mean plasma clearance is approximately 50 litres/hour (coefficient of variation 21.7%). As with other HMG-CoA reductase inhibitors, the hepatic uptake of rosuvastatin involves the membrane transporter OATP-C. This transporter is important in the hepatic elimination of rosuvastatin.

5.3 Preclinical safety data

Preclinical data reveal no special hazard for humans based on conventional studies of genotoxicity and carcinogenic potential.

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

Sunset Yellow

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 authorisation holder and Manufacturing Site
Marketing authorization holder:

INNOCIA LIFESCIENCES PVT. LTD.,

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

Manufacturing site address:

ATOZ Pharmaceutials Pvt.Ltd.,

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

India.

Local Technical Representative:

Wessex Pharmaceuticals Limited
Kenya

8. Marketing authorisation number

CTD9695

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