SUMMARY OF PRODUCT CHARACTERISTICS

(PRODUCT DATA SHEET)

1. Name of the Medicinal Product : ROSUVASTATIN CALCIUM TABLETS 20 mg

1.1 Product Name : AURITZ 20

1.2 Strength : 20 mg

1.3 Pharmaceutical Dosage Form : Solid oral dosage form - Tablet

2. Quality and Quantitative Composition :

2.1 Qualitative Declaration

INN Name:

IUPAC Name: bis[(E)-7-[4 (4-fluorophenyl)-6-isopropyl 2 [methyl (methylsulfonyl) amir pyrimidin-5-yl] (3R,5S) 3,5-dihydroxyhept-6-enoic acid] calcium salt

Ingredients	Reference
Rosuvastatin calcium	IHS
Tribasic Calcium phosphate (DC Grade)	USP-NF
Microcrystalline Cellulose (PH 102)	USP-NF
Butylated Hydroxy Toluene	USP-NF
Povidone K - 30	USP-NF
Croscarmellose Sodium	USP-NF
Colloidal silicon dioxide	USP-NF
Magnesium Stearate	USP-NF
Instacoat Universal white (IC-U-1308)	IHS
Purified Water	USP-NF

Quantitative Declaration

Ingredients	Reference*	Dosage (mg) / Tablet	Function
Rosuvastatin calcium	IHS	20.80	Active ingredient
Tribasic Calcium phosphate (DC Grade)	USP-NF	190.00	Diluent
Microcrystalline Cellulose (PH 102)	USP-NF	152.00	Diluent
Butylated Hydroxy Toluene	USP-NF	00.20	Antioxidant
Povidone K - 30	USP-NF	4.00	Binder
Croscarmellose Sodium	USP-NF	30.00	Disintegrant
Colloidal silicon dioxide	USP-NF	1.00	Glidant
Magnesium Stearate	USP-NF	2.00	Lubricant
Instacoat Universal white (IC-U-1308)	IHS	12.00	Coating agent
Purified Water	USP-NF	Q.S	Solvent

3. Pharmaceutical form:

Round shaped biconvex white colored smooth film coated tablets with a plain surface on both sides

4. Clinical Particulars:

4.1 Therapeutic indications:

Hyperlipidemia and Mixed Dyslipidemia Rosuvastatin is indicated as adjunctive therapy to diet to reduce elevated Total -C, LDL- C, ApoB, non-HDL-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 non - pharmacological interventions alone has been inadequate. Pediatric Patients 1 0 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 post - menarche, 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 or premature cardiovascular disease (CVD) or two or more other CVD risk factors.

Hypertriglyceridemia

Rosuvastatin is indicated as adjunctive therapy to diet for the treatment of adult patients with hypertriglyceridemia.

Primary Dysbetalipoproteinemia (Type Ill Hyperlipoproteinemia)

Rosuvastatin is indicated as an adjunct to diet for the treatment of patients with primary dysbetalipoproteinemia (Type Ill Hyperlipoproteinemia)

Homozygous Familial Hypercholesterolemia

Rosuvastatin is indicated as 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 hypercholesterolemia.

Slowing of the Progression of Atherosclerosis

Rosuvastatin is indicated as adjunctive therapy 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. Limitations of Use The effect of Rosuvastatin on cardiovascular morbidity and mortality has not been determined. Rosuvastatin has not been studied Fredrickson Type I and V dyslipidemias.

4.2 Posology and method of administration:

General Dosing Information

The dose range for Rosuvastatin is 5 to 40mg orally once daily. Rosuvastatin can be administered as a single dose at any time of day, with or without food. When initiating Rosuvastatin therapy or switching from another HMG-CoA reductase inhibitor therapy, the appropriate Rosuvastatin starting dose should first be utilized, and only then titrated according to the patients response and individualized goal of therapy. The 40mg dose of Rosuvastatin should be used only for those patients who have not achieved their LDL-C goal utilizing the 20mg dose.

Hyperlipidemia, Mixed Dyslipidemia, Hypertriglyceridemia, Primary Dysbetalipoproteinemia (Type Ill Hyperlipoproteinemia) and Slowing of the Progression of Atherosclerosis The recommended starting dose of Rosuvastatin is 10mg dose once daily.

For patients with marked hyperlipidemia (LDL-C > 190 mg / di) and aggressive lipid targets, a 20 mg starting dose may be considered. After initiation or upon titration of Rosuvastatin lipid levels should be analyzed within 2 to 4 weeks and the dosage adjusted accordingly.

Heterozygous Familial Hypercholesterolemia in Pediatric Patients (10to 17 years age)

The usual dose range of Rosuvastatin is 5-20 mg/day; the maximum recommended dose is 20 mg/day (doses greater than 20mg have not been studied in this patient population). 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 Rosuvastatin is 20mg once daily. Response to therapy should be estimated from pre-aphereses LDL-C levels. Dosage in Asian Patients Initiation of Rosuvastatin therapy with 5 mg once daily should be considered for Asian patients.

Use with Cyclosporine or Lopinavir / Ritonavir :

In patients taking cyclosporine, the dose of Rosuvastatin should be limited to 5mg once daily. In patients taking a combination of lopinavir and ritonavir, the dose of Rosuvastatin should be limited to 10mg once daily.

Concomitant Lipid-Lowering Therapy The risk of skeletal muscle effects may be enhanced when Rosuvastatin is used in combination with niacin or fenofibrate; a reduction in Rosuvastatin is used in combination with gemfibrozil, the dose of Rosuvastatin should be limited to 10mg daily. Dosage in Patients with Severe Renal Impairment

For patients with severe renal impairment (CI,<30 mL/min/1.73m) not on hemodialysis, dosing of Rosuvastatin should be started at 5mg once daily and not exceed 10mg once daily.

4.3 Contraindications:

Rosuvastatin is contraindicated in the following conditions:

- Patients with a known hypersensitivity to any component of this product. Hypersensitivity reactions including rash, pruritus, urticaria and angioedema have been reported with Rosuvastatin
- Patients with active liver disease, which may include unexplained persistent elevations of hepatic transaminase levels.
- Women who are pregnant or may become pregnant. Because HMG-CoA reductase inhibitors decrease cholesterol synthesis and possibly the synthesis of other biologically active substances derived from cholesterol, Rosuvastatin may cause fetal harm when administered to pregnant women. Additionally, there is no apparent benefit to therapy during pregnancy, and safety in pregnant women has not been established. If the patient becomes pregnant while taking this drug, the patient should be apprised of the potential hazard to the fetus and the lack of known clinical benefit with continued use during pregnancy.
- Nursing mothers. Because another drug in this class passes into breast milk, and because HMG-CoA reductase inhibitors have the potential to cause serious adverse reactions in nursing infants, women who require Rosuvastatin treatment should be advised not to nurse their infants.

4.4 Special warning and precautions for use :

Skeletal Muscle Effects

Cases of myopathy and rhabdomyolysis with acute renal failure secondary to myoglobinuria have been reported with HMG - CoA reductase inhibitors including Rosuvastatin These risks can occur at any dose level, but are increased at the highest dose (40mg).

Rosuvastatin should be prescribed with caution in patients with predisposing factors for myopathy.

The risk of myopathy during treatment with Rosuvastatin may be increased with concurrent administration of some other lipid-lowering therapies (fibrates or niacin), gemfibrozil, cyclosporine, or lopinavir / ritonavir. Rosuvastatin should be discontinued if markedly elevated creatinine kinase levels occur or myopathy is diagnosed or suspected. Rosuvastatin therapy should also be temporarily withheld in any patient with an acute, serious condition suggestive of myopathy or predisposing to the development of renal failure secondary to rhabdomyolysis

(e.g. sepsis, hypotension, dehydration, major surgery, trauma, severe metabolic, endocrine, and electrolyte disorders, or uncontrolled seizures). All patients should be advised to promptly report unexplained muscle pain, tenderness, or weakness, particularly if accompanied by malaise or fever.

Liver Enzyme Abnormalities and Monitoring

It is recommended that liver enzyme tests be performed before and at 12 weeks following both the initiation of therapy and any elevation of dose, and periodically (e.g. semiannually) thereafter. Increases in serum transaminases [AST (SGOT) or ALT (SGPT) have been reported with HMG - CoA reductase inhibitors, including Rosuvastatin Patients who develop increased transaminase levels should be monitored until the abnormalities have resolved. Should an increase in ALT or AST of > 3 times ULN persist, reduction of dose or withdrawal of Rosuvastatin is recommended. Rosuvastatin should be used with caution in patients who consume substantial quantities of alcohol and /or have a history of chronic liver disease.

Proteinuria and Hematuria

Dipstick-positive proteinura and microscopic hematuria were observed among Rosuvastatin treated patients. These findings were more frequent in patients taking Rosuvastatin 40mg, when compared to lower doses of Rosuvastatin or comparator HMG-CoA reductase inhibitors, though it was generally transient and was not associated with worsening renal function. Although the clinical significance of this finding is unknown, a dose reduction should be considered for patients on Rosuvastatin therapy with unexplained persistent proteinuria and/or hematuria during routine urinalysis testing.

Endocrine Effects

Rosuvastatin alone does not reduce basal plasma cortisol concentration or impair adrenal reserve, however, caution should be exercised if Rosuvastatin is administered concomitantly with drugs that may decrease the levels or activity of endogenous steroid hormones such as ketoconazole, spironolactone, and cimetidine.

4.5 Interaction with other medicinal products and other forms of Interactions:

Cyclosporine

Cyclosporine significantly increased rosuvastatin exposure. Therefore, in patients taking cyclosporine; therapy should be limited to Rosuvastatin 5 mg once daily.

Gemfibrozil

Gemfibrozil significantly increased rosuvastatin exposure. Therefore, combination therapy with Rosuvastatin and gemfibrozil should be avoided. If used, do not exceed Rosuvastatin 10mg once daily.

Lopinavir / Ritonavir

The combination of lopinavir and ritonavir significantly increased exposure. Therefore, in patients taking a combination of lopinavir and ritonavir, the dose of Rosuvastatin should be limited to 10mg once daily. The effect of the other protease inhibitors on rosuvastatin pharmacokinetics has not been examined.

Coumarin Anticoagulants

Rosuvastatin significantly increased International Normalized Ratio (INR) in patients receving coumarin anticoagulants. Therefore, caution should be exercised when coumarin anticoagulants are

given in conjunction with Rosuvastatin. 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.

Niacin

The risk of skeletal muscle effects may be enhanced when Rosuvastatin is used in combination with niacin; a reduction in Rosuvastatin dosage should be considered in this setting.

Fenofibrate

When Rosuvastatin was coadministered with fenofibrate no clinically significant increase in the AUC of rosuvastatin or fenofibrate was observed. The benefit of further alterations in lipid levels by the combined use of Rosuvastatin with fibrates should be carefully weighed against the potential risks of this combination.

4.6 Pregnancy and lactation:

Teratogenic effects: Pregnancy Category X. Rosuvastatin is contraindicated in women who are or may become pregnant. Serum cholesterol and triglycerides increase during normal pregnancy, and cholesterol products are essential for fetal development. Atherosclerosis is a chronic process and discontinuation of lipid-lowering drugs during pregnancy should have little impact on long-term outcomes of primary hyperlipidemia therapy.

There are no adequate and well-controlled studies of Rosuvastatin in pregnant women. There have been rare reports of congenital anomalies following intrauterine exposure to HMG-CoA reductase inhibitors. Rosuvastatin may cause fetal harm when administered to a pregnant woman. If the patient becomes pregnant while taking Rosuvastatin, the patient should be apprised of the potential risks to the fetus and the lack of known clinical benefit with continued use during pregnancy.

Nursing Mothers

It is not known whether rosuvastatin is excreted in human milk, but a small amount of another drug in this class does pass into breast milk.

Because another drug in this class passes into human milk and because HMG-CoA reductase inhibitors have a potential to cause serious adverse reactions in nursing infants, women who require Rosuvastatin treatment should be advised not to nurse their infants.

Pediatric Use

Although not all adverse reactions identified in the adult population have been observed in clinical trials of children and adolescent patients, the same warnings and precautions for adults should be considered for children and adolescents. Doses of Rosuvastatin greater than 20mg have not been studied in the pediatric population.

Geriatric Use

Elderly patients are at higher risk of myopathy and Rosuvastatin should be prescribed with caution in the elderly use.

Renal Impairment

Rosuvastatin exposure is not influenced by mild to moderate renal impairment; however, exposure to rosuvastatin is increased to a clinically significant extent in patients with severe renal impairment who are not receiving hemodialysis. Rosuvastatin dosing should be adjusted in patients with severe renal impairment not requiring hemodialysis and Clinical Pharmacology.

Hepatic Impairment

Rosuvastatin is contraindicated in the patients with active liver disease, which may include unexplained persistent elevations of hepatic transaminase levels. Chronic alcohol

liver disease is known to increase rosuvastatin exposure; Rosuvastatin should be used with caution in these patients.

Asian Patients

Pharmacokinetic studies have demonstrated an approximate 2-fold increase in median exposure to Rosuvastatin in Asian subjects when compared with Caucasian controls. Rosuvastatin dosage should be adjusted in Asian patients.

4.7 Effects on ability to drive and use machine:

Studies to determine the effect of rosuvastatin on the ability to drive and use machines have not been conducted. However, 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.

Adverse reactions :

The following serious adverse reactions are discussed in

greater detail in other sections of the label:

• Rhabdomyolysis with myoglobinuria and acute renal

failure and myopathy (including myositis)

• Liver enzyme abnormalities

The most commonly reported adverse reactions with

Rosuvastatin:

• headache

• myalgia

• abdominal pain

• asthenia nausea

Overdose and special antidotes :

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. Hemodialysis does not significantly enhance clearance of rosuvastatin. However, no specific symptoms of an overdose have been reported.

5. Pharmacological Properties:

5.1 Pharmacodynamic Properties:

Pharmacotherapeutic group: HMG-CoA reductase inhibitors , ATC code: C10AA07

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 of cholesterol. 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.

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. Both Cmax and AUC increased in

approximate proportion to Rosuvastatin dose. The absolute bioavailability of Rosuvastatin is approximately 20%.Administration of Rosuvastatin with food did not affect the AUC of Rosuvastatin. The AUC of Rosuvastatin does not differ following evening or morning drug administration.

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.

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%).The elimination half-life (t,) of Rosuvastatin is approximately 19hours. After an intravenous dose, approximately 28% of total body clearance was via the renal route and 72% by the hepatic route.

5.3 Preclinical safety Data:

Not available

6. Pharmaceutical Particulars:

6.1 List of excipients:

Tribasic Calcium Phosphate USP/NF, Microcrystalline cellulose (PH 102) USP/NF, Butylated Hydroxy Toluene USP/NF, Povidone K-30 USP/NF, Croscarmellose sodium USP/NF, Colloidal silicon dioxide USP/NF, Magnesium stearate USP/NF, Instacoat Universal white IH, Purified water USP.

6.2 Incompatibilities: Not applicable

6.3 Shelf life:

24 Months

6.4 Special precautions for storage:

• Keep out of reach of children

• Protect from light and moisture

• Store below 30°C in a dry place

6.5 Nature and contents of container:

Available as packs of 3x10's

6.6 Special precautions for disposal and other handling:

Dutasteride is absorbed through the skin, therefore contact with leaking capsules must be avoided. If contact is made with leaking capsules, the contact area should be washed immediately with soap and water. Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. Marketing Authorization Holder and manufacturing site address:

Marketing Authorization Holder:

Mega Lifesciences Nigeria Limited,

Metal House, Plot No.6,

Cocoa Industrial Road,

Ogba Industrial Layout,

Ogba, Ikeja, Lagos State

Manufacturing site address:

MSN LABORATORIES PRIVATE LIMITED (Formulations Division)

Plot No. 42, Anrich Industrial Estate, Bollaram,

Sangareddy District - 502 325, Telangana, India.

8. Marketing Authorization Number:A4-7497

9. Date of first authorization / renewal of the authorization : october 2017

10. Date of revision of the text: --