SUMMARY PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT:
Roviros 10mg

2. QUALITATIVE AND QUANTITATIVE COMPOSITION:
Each film coated tablet contains:
Rosuvastatin Calcium eq. to Rosuvastatin…….10mg

For the full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM:
Tablet
White to off white colored film coated, spindle shaped tablet. Both sides plain.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications
Hyperlipidemia and Mixed Dyslipidemia:
Roviros (Rosuvastatin) is indicated 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 non-pharmacological interventions alone has been inadequate.

Hypertriglyceridemia:
Roviros (Rosuvastatin) is indicated as adjunctive therapy to diet for the treatment of adult patients with hypertriglyceridemia.

Homozygous Familial Hypercholesterolemia:
Roviros (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: Roviros (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. Prior to initiating therapy with Rosuvastatin, secondary causes of hypercholesterolemia (e.g. poorly controlled diabetes mellitus, hypothyroidism, nephrotic syndrome, dysproteinaemias, obstructive liver disease, other drug therapy) should be identified and treated.

4.2 Posology and method of administration
General Dosing Information: The dose range for Roviros is 5 to 40mg orally once daily. Roviros can be administered as a single dose at any time of day, with or without food. When

initiating Roviros therapy or switching from another HMG-CoA reductase inhibitor therapy, the appropriate Roviros starting dose should first be utilized, and only then titrated according to the patient's response and individualized goal of therapy.
The 40mg dose of Roviros should be used only for those patients who have not achieved their LDL-C goal utilizing the 20mg dose.

Hyperlipidemia, Mixed Dyslipidemia, Hypertriglyceridemia and Slowing of the Progression of Atherosclerosis: The recommended starting dose of Roviros is 10mg once daily. For patients with marked hyperlipidemia (LDL-C > 190mg/dl) and aggressive lipid targets, a 20mg starting dose may be considered. After initiation or upon titration of Roviros, lipid levels should be analyzed within 2 to 4 weeks and the dosage adjusted accordingly.

Homozygous Familial Hypercholesterolemia: The recommended starting dose of Roviros is 20mg once daily. Response to therapy should be estimated from pre-apheresis LDL-C levels.

Use in children: Experience is limited to a small number of children (aged 8 years and above) with homozygous familial hypercholesterolemia.

Use in the elderly: The usual dose range applies.

Dosage in patients with renal insufficiency: The usual dose range applies in patients with mild to moderate renal impairment.
For patients with severe renal impairment the dose of Roviros should be started at 5mg once daily and not exceed 10mg once daily.

4.3 Contraindications:
Roviros is contra-indicated in patients with hypersensitivity to any component of this product. Rosuvastatin is contra-indicated in patients with active liver disease or persistent, unexplained elevations in transaminases.
Pregnancy and Lactation: Roviros is contra-indicated in pregnancy and lactation.

4.4 Special warnings and precautions for use:
Statins should not be given to patients with active liver disease or unexplained persistently raised serum aminotransferase concentrations.
They should be avoided during pregnancy since there is a possibility that they could interfere with fetal sterol synthesis; there have been a few reports of congenital abnormalities associated with statins. They should be discontinued if marked or persistent increases in serum aminotransferase or creatine phosphokinase concentrations occur, or if myopathy is diagnosed. Rosuvastatin should be used with caution in patients with severe renal impairment.

4.5 Interaction with other medicinal products and other forms of interaction:
The most serious consequence of drug interactions with statins is the development of myopathy or rhabdomyolysis. Drugs that can cause myopathy when given alone increase the

risk of myopathy with all statins; these drugs include fibric acid derivatives (fibrates or gemfibrozil), and nicotinic acid. The risk of myopathy is also increased by drugs that increase the plasma levels of statins by inhibiting their metabolism. Rosuvastatin under goes limited metabolism, principally by the cytochrome P450 isoenzyme CYP2C9, and may not have the same interactions with enzyme inhibitors as simvastatin. However, increased Rosuvastatin plasma concentrations have been reported with cyclosporine and, to a lesser extent, with gemfibrozil, and such combinations should be avoided. If they must be given together, lower doses of Rosuvastatin should be used. Statins may also have effects on other drugs. Bleeding and increases in prothrombin time have been reported in patients taking with coumarin anticoagulants.

4.6. Fertility, Pregnancy and Lactation

Carcinogenesis, Mutagenesis, Impairment of Fertility

In a 104-week carcinogenicity study in rats at dose levels of 2, 20, 60, or 80 mg/kg/day by oral
gavage, the incidence of uterine stromal polyps was significantly increased in females at 80 mg/kg/day at systemic exposure 20 times the human exposure at 40 mg/day based on AUC. Increased incidence of polyps was not seen at lower doses.

In a 107-week carcinogenicity study in mice given 10, 60, 200 mg/kg/day by oral gavage, an increased incidence of hepatocellular adenoma/carcinoma was observed at 200 mg/kg/day at systemic exposures 20 times the human exposure at 40 mg/day based on AUC. An increased incidence of hepatocellular tumors was not seen at lower doses.

Rosuvastatin was not mutagenic or clastogenic with or without metabolic activation in the Ames test with *Salmonella typhimurium* and *Escherichia coli*, the mouse lymphoma assay, and the chromosomal aberration assay in Chinese hamster lung cells. Rosuvastatin was negative in the *in vivo* mouse micronucleus test.

In rat fertility studies with oral gavage doses of 5, 15, 50 mg/kg/day, males were treated for 9 weeks prior to and throughout mating and females were treated 2 weeks prior to mating and throughout mating until gestation day 7. No adverse effect on fertility was observed at 50 mg/kg/day (systemic exposures up to 10 times the human exposure at 40 mg/day based on AUC).

In testicles of dogs treated with Rosuvastatin at 30 mg/kg/day for one month, spermatidic giant cells were seen. Spermatidic giant cells were observed in monkeys after 6-month treatment at 30 mg/kg/day in addition to vacuolation of seminiferous tubular epithelium. Exposures in the dog were 20 times and in the monkey 10 times the human exposure at 40 mg/day based on body surface area. Similar findings have been seen with other drugs in this class.

4.7. Effects on ability to drive and use machines:

None known.

4.8. Undesirable effects:

The commonest adverse effects of therapy with statins are gastrointestinal disturbances. Other adverse effects reported include headache, skin rashes, dizziness, blurred vision,

insomnia, and dysgeusia. Reversible increases in serum aminotransferase concentrations may occur and liver function should be assessed before treatment is initiated and then monitored periodically until one year after the last elevation in dose. Hepatitis and pancreatitis have been reported.
Hypersensitivity reactions including anaphylaxis and angioedema have also occurred.
Myopathy, characterized by myalgia and muscle weakness and associated with increased creatine phosphokinase concentrations, has been reported, especially in patients taking statins concurrently with cyclosporin, fibric acid derivatives, or nicotinic acid, rarely, rhabdomyolysis with acute renal failure may develop.

Reporting of suspected adverse reactions:
Reporting suspected adverse reactions after authorization of the medicinal product is important as it allows continued monitoring of the benefit–risk balance of the medicinal product. Healthcare professionals are requested to report any suspected adverse reactions to the marketing authorization holder or, where applicable, via the national reporting system https://pv.pharmacyboardkenya.org/

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. Hemodialysis does not significantly enhance clearance of rosuvastatin.

5. PHARMACOLOGICAL PROPERTIES:

5.1 Pharmacodynamic properties:
Rosuvastatin is a selective, potent 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. Triglycerides (TG) and cholesterol in the liver are incorporated, with apolipoprotein B (ApoB), into very low-density lipoprotein (VLDL) and released into the plasma for delivery to peripheral tissues.
VLDL particles are TG-rich. Cholesterol rich low-density lipoprotein (LDL) is formed from VLDL and is cleared primarily through the high affinity LDL receptor in the liver.
Rosuvastatin produces its lipid modifying effects in two ways; it 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. High density lipoprotein (HDL), which contains ApoA-1 is involved, amongst other things, in transport of cholesterol from tissues back to the liver (reverse cholesterol transport).

5.2 Pharmacokinetic properties:
Rosuvastatin is incompletely absorbed from the gastro-intestinal tract, with a bioavailability of about 20%. Peak plasma concentrations are achieved about 5 hours after an oral dose. It is taken up extensively by the liver, its primary site of action, and undergoes limited metabolism, mainly by the cytochrome P450 isoenzyme CYP2C9. It is about 90% bound to plasma proteins. The plasma elimination half-life of Rosuvastatin is about 19 hours.

Approximately 90% of an oral dose of Rosuvastatin is excreted in the feces, including absorbed and non-absorbed drug, and the remainder is excreted in the urine; about 5% of a dose is excreted unchanged in urine.

5.3 Preclinical safety data:
Preclinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, genotoxicity and carcinogenicity potential. Specific tests for effects on hERG have not been evaluated. Adverse reactions not observed in clinical studies, but seen in animals at exposure levels similar to clinical exposure levels were as follows: In repeated-dose toxicity studies histopathologic liver changes likely due to the pharmacologic action of rosuvastatin were observed in mouse, rat, and to a lesser extent with effects in the gall bladder in dogs, but not in monkeys. In addition, testicular toxicity was observed in monkeys and dogs at higher dosages. Reproductive toxicity was evident in rats, with reduced litter sizes, litter weight and pup survival observed at maternally toxic doses, where systemic exposures were several times above the therapeutic exposure level.

6. PHARMACEUTICAL PARTICULARS:
6.1 List of excipients
Polyvinyl Pyrolidone K-30
Lactose Monohydrate
Maize Starch
Ac-Di-Sol
Talcum Powder
Magnesium Stearate
Isopropyl Alcohol

Coating Material
HPMC 606
Titanium Dioxide
PEG # 6000
De-ionized Water

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. Keep out of the reach of children. To be sold on the prescription of a registered medical practitioner only

6.5 Nature and contents of container:

Roviros 10mg Tablet is available in alu-alu blister with secondary carton of pack is of white bleach board with water base.

6.6 Special precautions for disposal and other handling
No special requirements

7. MARKETING AUTHORISATION HOLDER:
Nabiqasim Industries (Pvt.) Ltd.
17/24, Korangi Industrial Area,
Korangi,
Karachi – Pakistan.

8. MARKETING AUTHORISATION NUMBER:
H2022/CTD6289/1974ER

9. DATE OF FIRST AUTHORIZATION/RENEWAL OF THE AUTHORISATION:
22/04/2022

10. DATE OF REVISION OF THE TEXT:
22/04/2022